STIs:
WHAT'S ON THE HORIZON

John G. Bartlett
Johns Hopkins University
School of Medicine

Conflicts -- None

STIs:
WHAT'S ON THE HORIZON

Overview

Epidemiology

Gonorrhea

HIV/AIDS

Hepatitis C

Human Papilloma Virus

Conclusions

STIs: STATE OF THE STATE AND STATE OF THE DISEASE

- ***Chlamydia trachomatis***
- ***Neisseria gonorrhoeae***
- ***Treponema pallidium***
- **Human Immunodeficiency virus**

  (HBV, HCV, HPV, CMV, HSV, HAV, MCV, Crabs, Scabies, Mycoplasma)

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- ***Treponema pallidium***
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  (HBV, HCV, HPV, CMV, HSV, HAV, MCV, Crabs, Scabies, Mycoplasma)

HOT TOPICS: STIs

HIV/AIDS

- Prevention
- Test → Engage care

N. gonorrhoeae

- Resistance

HPV

- Vaccine

(Hepatitis C)

- Test
- Treat

STIs:
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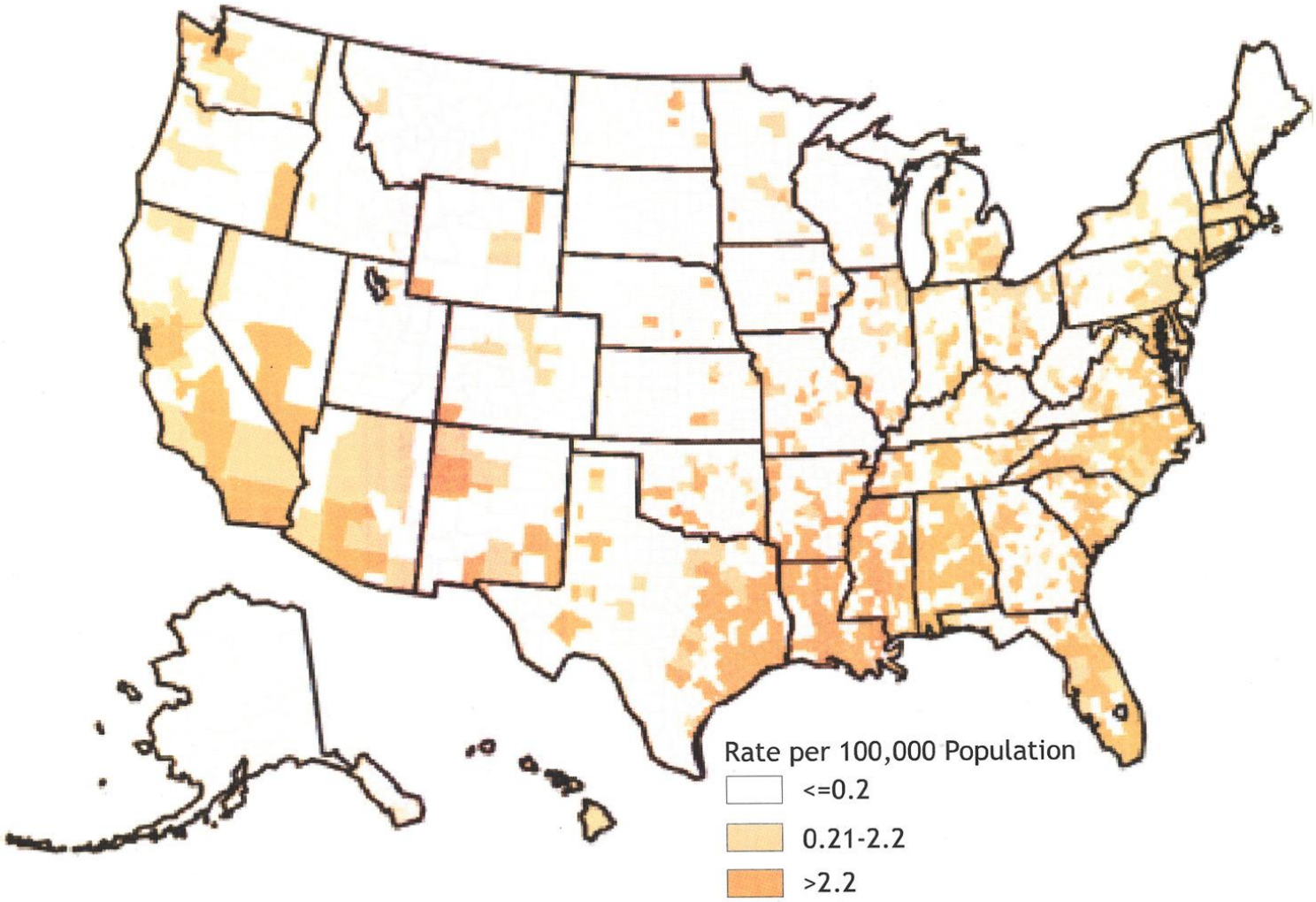
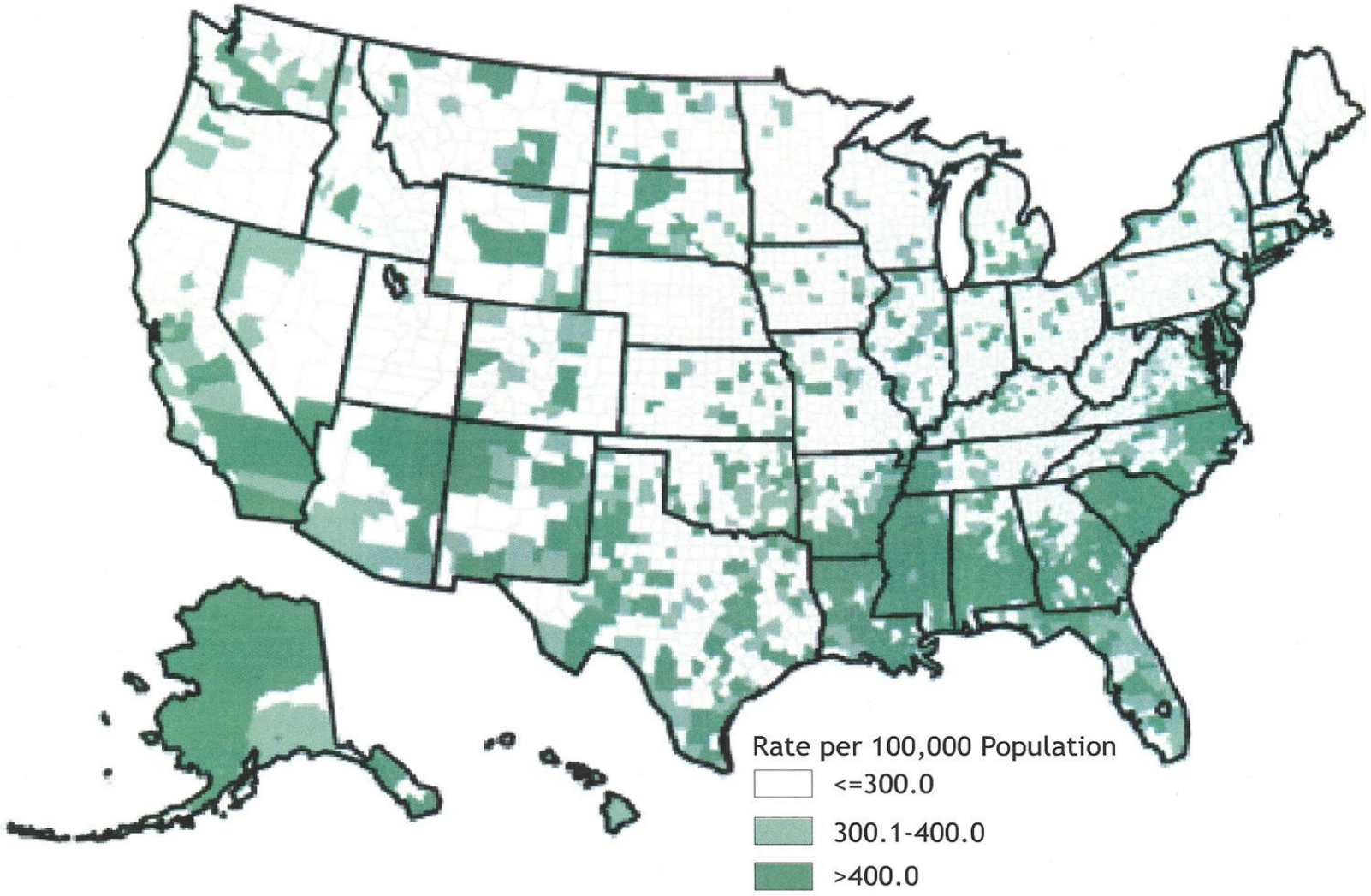
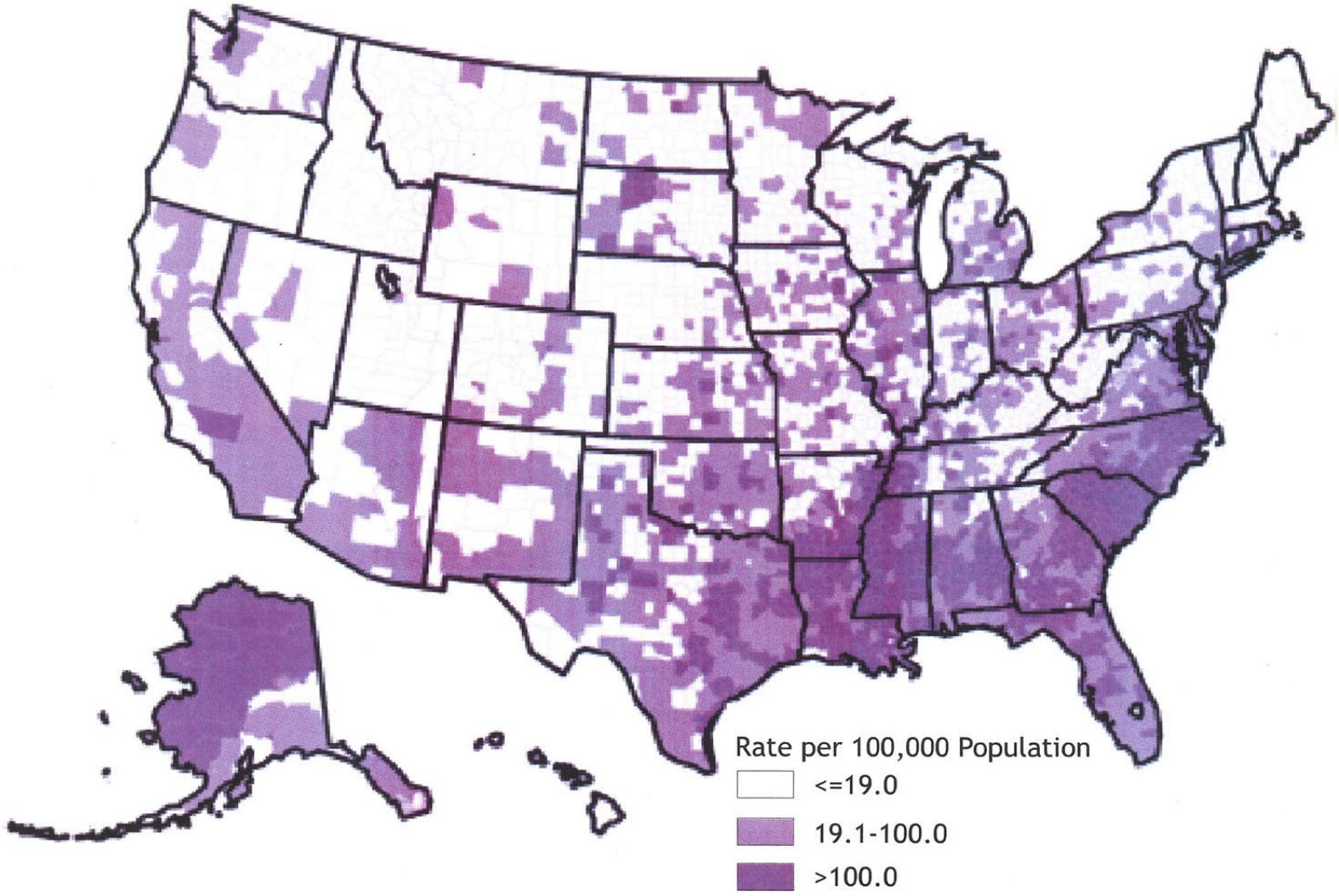
STD RATES BY GEOGRAPHIC LOCATION – SYPHILIS 2009



STD RATES BY GEOGRAPHIC LOCATION -- CHLAMYDIA 2009



STD RATES BY GEOGRAPHIC LOCATION -- GONORRHEA



STI RATES* AND RANKINGS: Maryland and US 2010

	US	MD	Rank
AIDS	10.8	22.1	#2
Syphilis congenital	8.7	28.7	#2
Syphilis 1 & 2	4.5	5.8	#7
GC	101	130	#11
C. trachomatis	426	460	#14

*Rate,100,000/pop.

STD RATES: Maryland Trends*

	2002	2007	2011	Change (10 yr)
C. trachomatis	314	412	489	+26%
N. gonorrhoea	174	121	111	-36%
T. pallidum	4.2	6.1	7.8	+86%**

*/100,000 population

**Baltimore increase 19 → 38

Source: Center for STD, DHMH & BCHD

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The Elephant in the Room: GC Resistance

Rates: 1976-96↓76%

1996-2009 Plateau

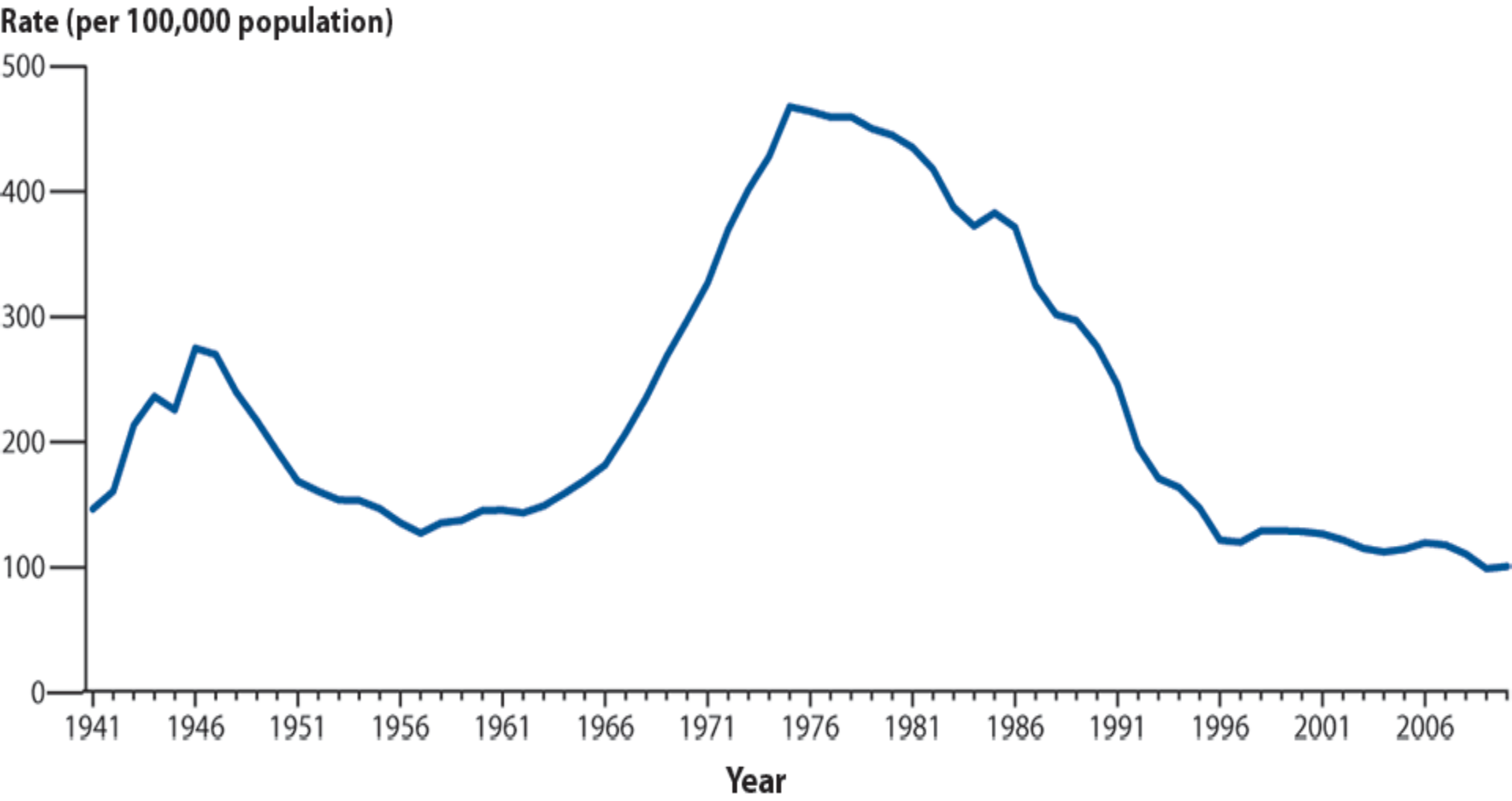
2010-2011 ↑ 2.8%

Demographics – AA:White = 18.7

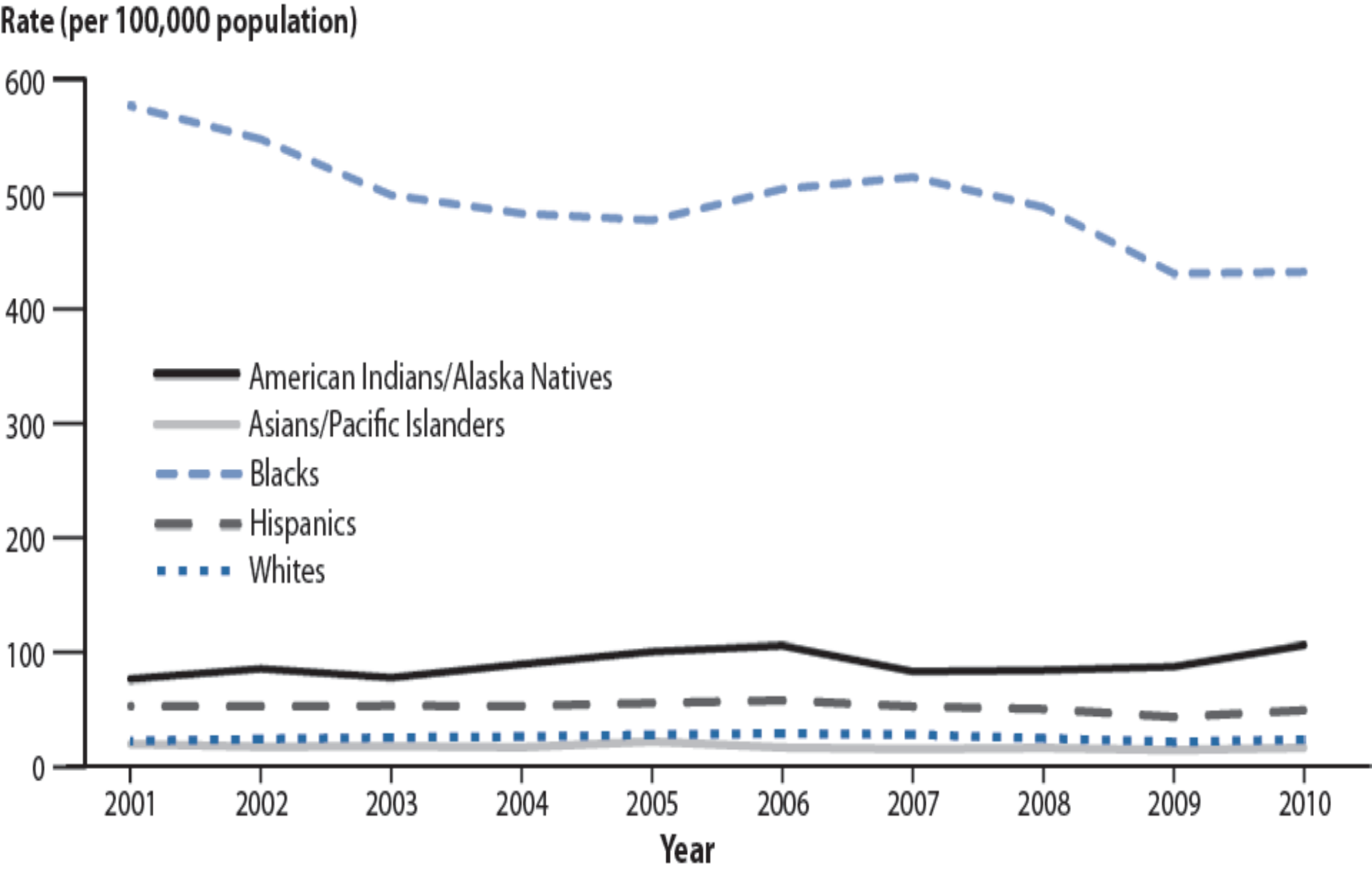
Resistance

- **Ceftriaxone: Only drug left**
- **Cefixime, azithro or quinolones resistance – MSM**

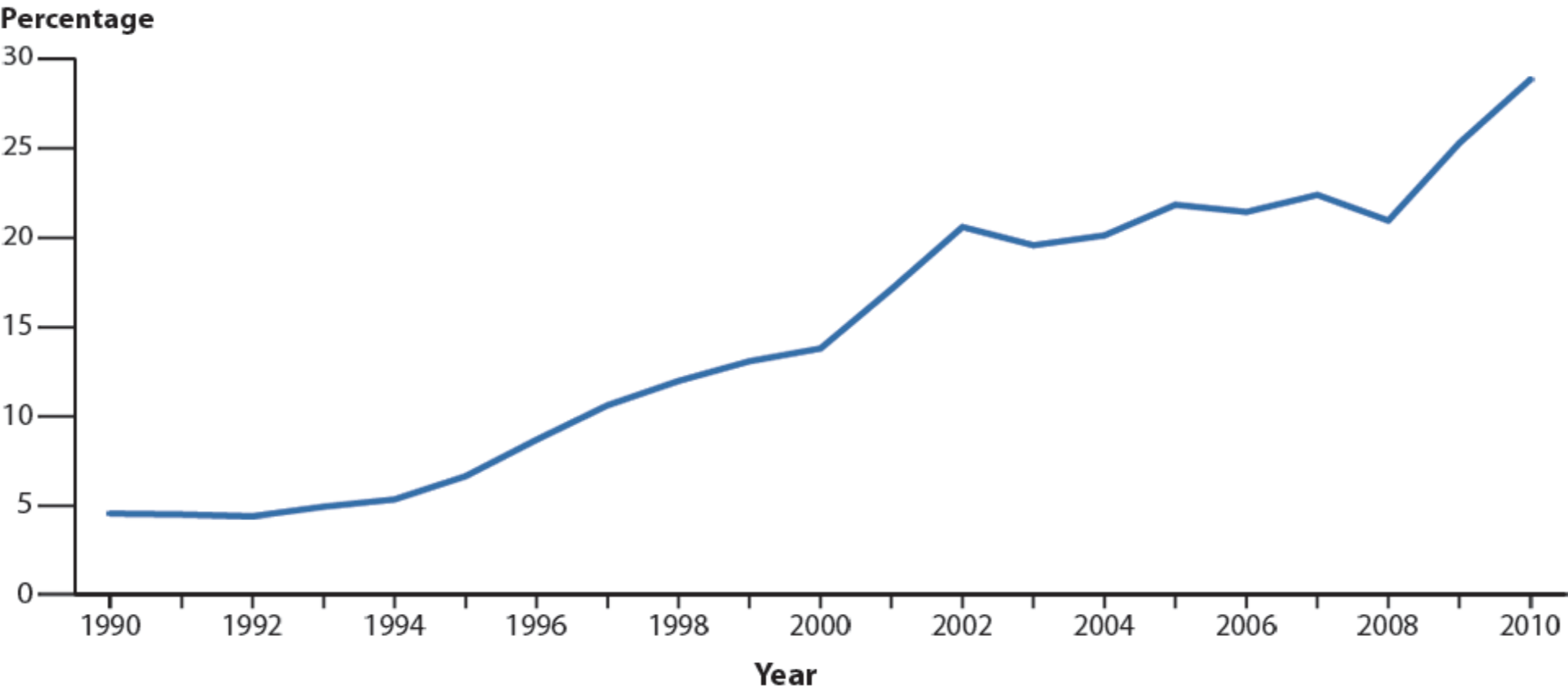
Gonorrhea—Rates, United States, 1941–2010



Gonorrhea—Rates by Race/Ethnicity, United States, 2001–2010

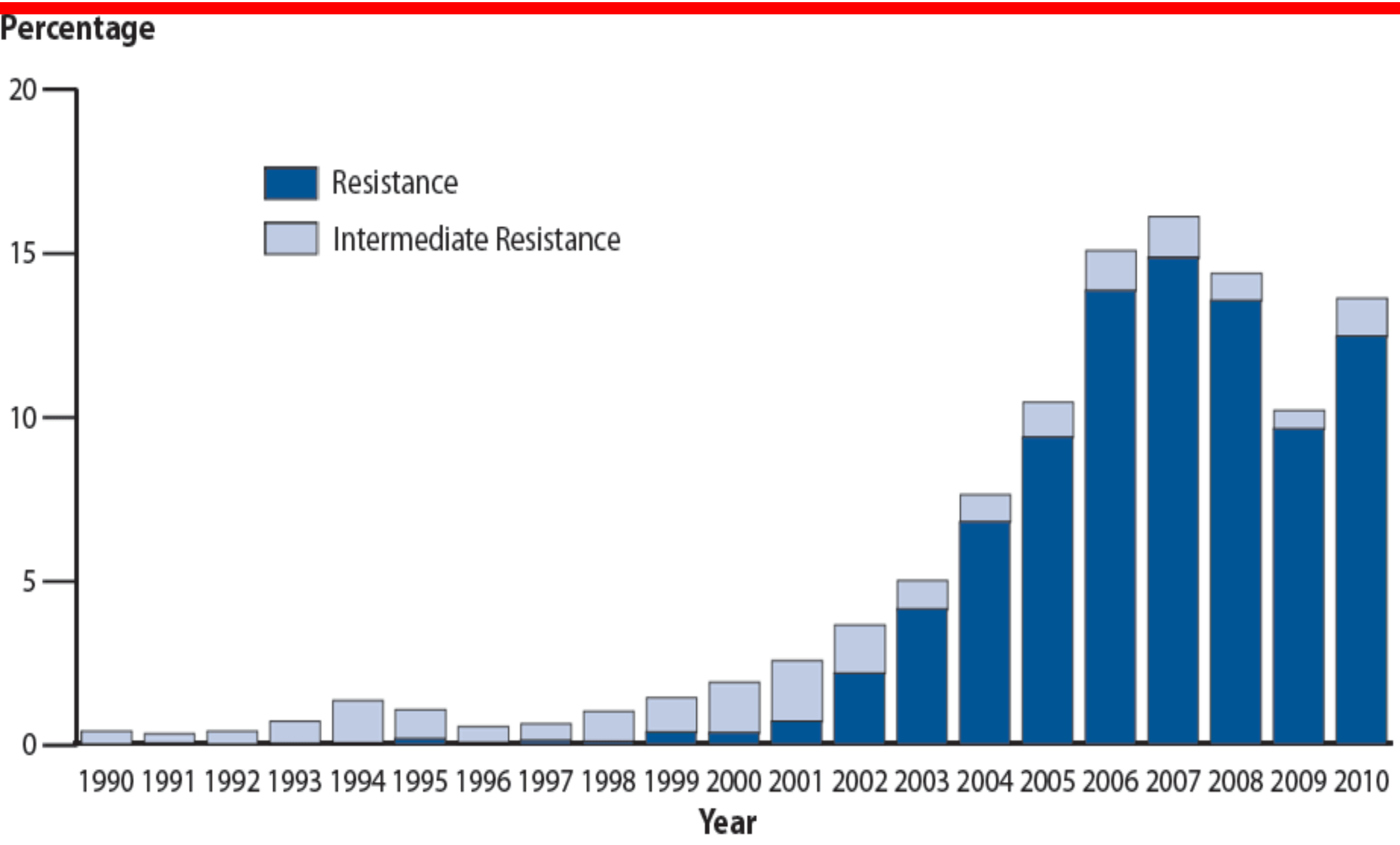


Gonococcal Isolate Surveillance Project (GISP)—Percentage of Urethral *Neisseria gonorrhoeae* Isolates Obtained from MSM* Attending STD Clinics, 1990–2010



* MSM = men who have sex with men.

Gonococcal Isolate Surveillance Project (GISP)—Percentage of *Neisseria gonorrhoeae* Isolates with Resistance or Intermediate Resistance to Ciprofloxacin, 1990–2010



EMERGING THREAT OF GONOCCAL INFECTION

(Bolan G. NEJM 2012;366:485)

Surveillance: Second most common reportable disease (600,000/yr)

Risk: "Marginalized" – AA, MSM

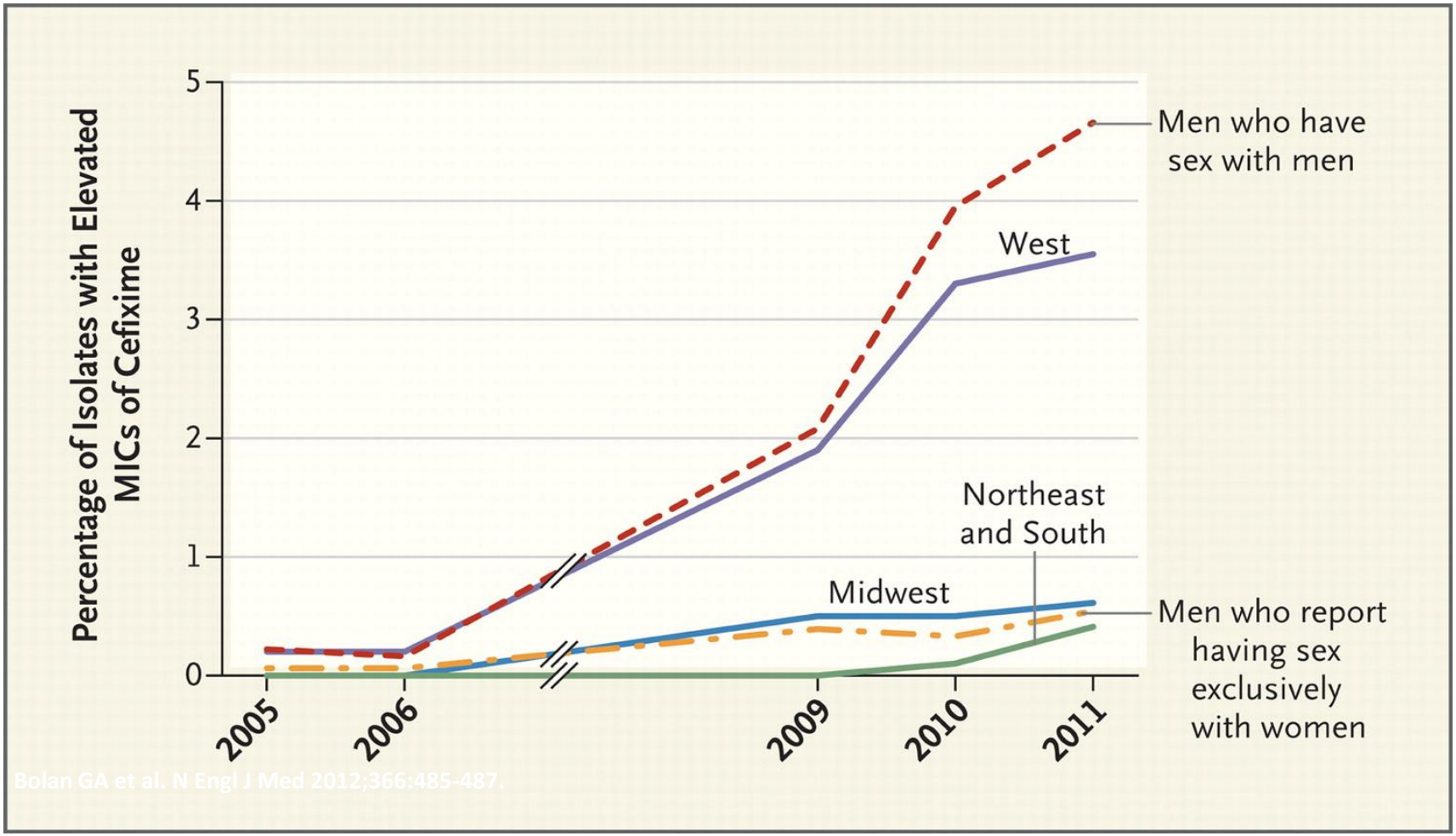
Resistance: "Always" develops

- Sulfanilamide – 1940's
- Penicillin and tetra – 1980
- Fluoroquinolones – 2007
- Cephalosporins, 3rd generation – MIC increased 17 fold 2006-11

Concerns: 1) Must rebuild labs for sensitivity testing (and pay for it) and 2) Spectinomycin and 3) Vaccine ?

RESISTANT *N. GONORRHOEAE* BY LOCATION, RISK AND YEAR

(Bolan G. NEJM 2012;366:485)



RESISTANCE: NEW THREATS

GNB – Carbapenems, etc

MRSA – Vancomycin

***N. gonorrhoea* – Cefixime, FQ**

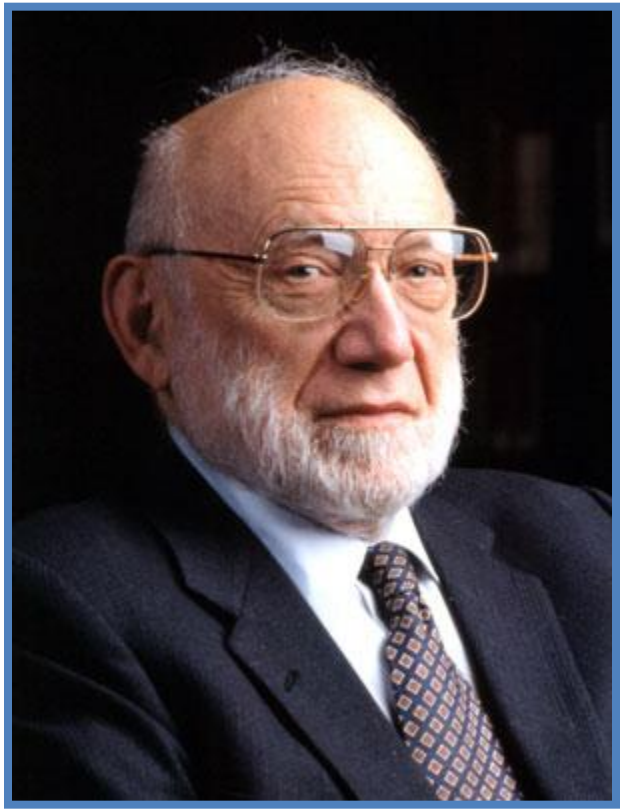
Influenza – Oseltamivir

***M. tuberculosis* – Rif, INH**

Malaria – Artemisinin

Cholera – ESBL, FQ

"The future of humanity and microbes will likely evolve as…episodes of our wits versus their genes."



Nobel Laureate
Joshua Lederberg
Science 2000;288:287

Discovery of highly resistant bacteria in Lechuguilla Cave indicating age >3.5 million years (Wright G. PLoS One – in press)

THE HISTORY OF INFECTIOUS DISEASE 2020

2000 BC: Eat this root – it heals

1000 AD: Roots are heathen – Say this prayer

1850 AD: Prayer is superstitious, Drink this potion

1940 AD: That potion is snake oil – Penicillin is the miracle

1985 AD: Penicillin no longer works – This new antibiotic is better

2020 AD: Those antibiotics don't work anymore – eat this root

N. gonorrhoeae: TREATMENT

1937: Sulfonamides

1940: Penicillin

1972: Pen dose ↑ and probenecid

1987: Sentinel surveillance

1990 – 08: Resistance

2006: Ceftriaxone, Cefixime, Cipro/levo/Oflox +Azitho/Doxy

Current: Ceftriazone 250 mg IM + Azithro 1 gm or doxy 100 bid x 7 d

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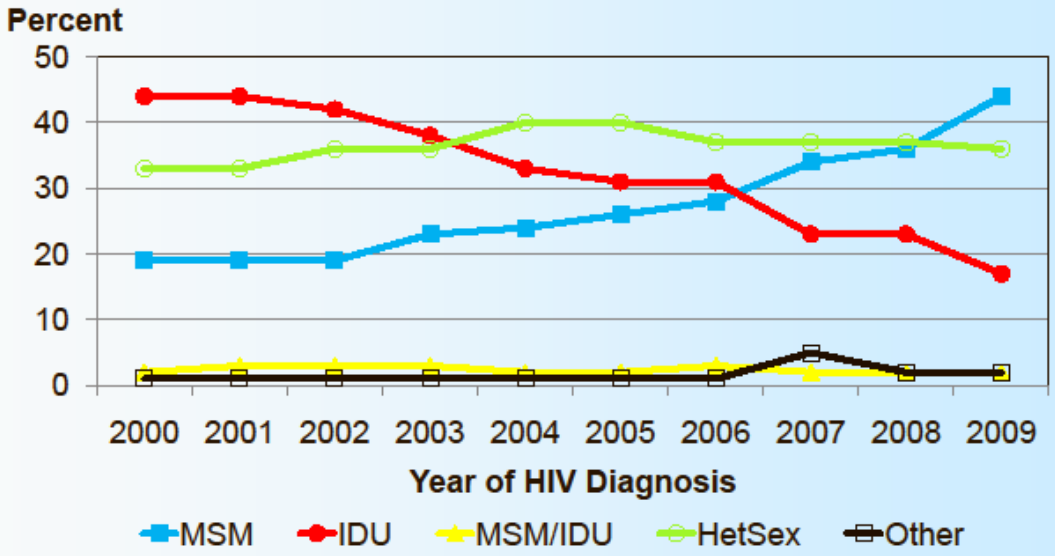
HIV/AIDS: MARYLAND

Reported HIV Diagnosis Trends by Exposure Category

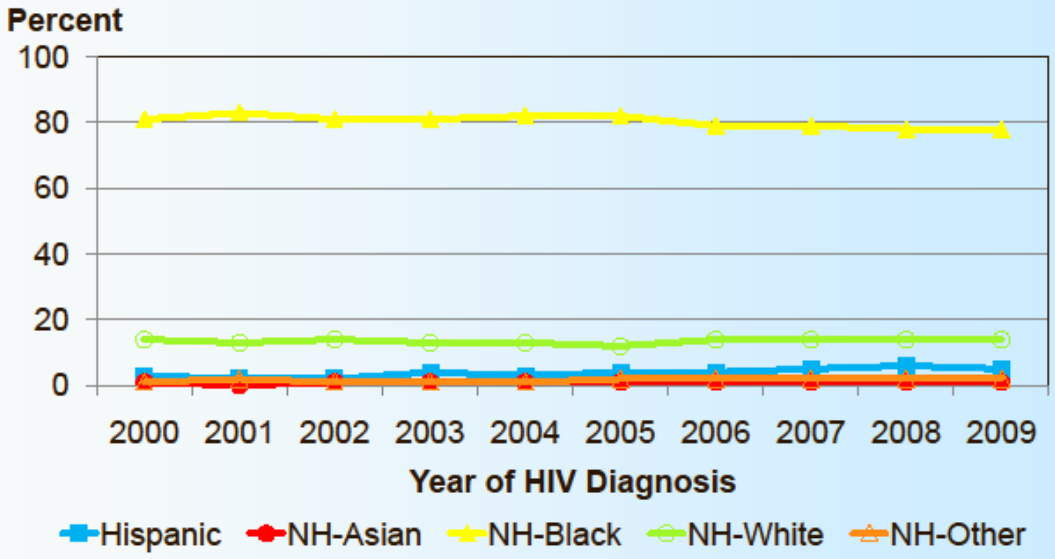


Using data as reported through 12/31/2010

Maryland Infectious Disease and Environmental Health Administration
March 3, 2011
25

HIV/AIDS: MARYLAND

Reported HIV Diagnosis Trends by Race/Ethnicity

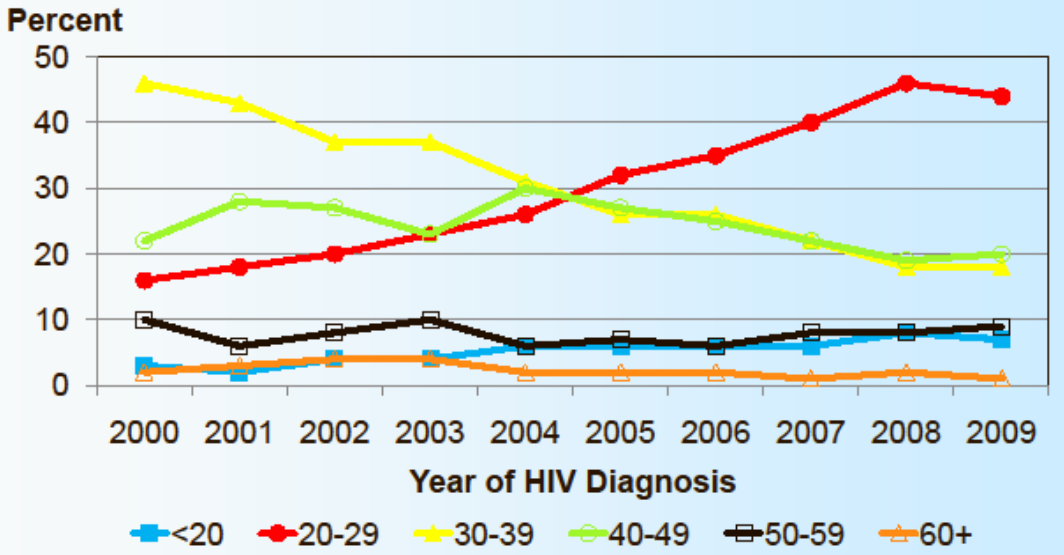


Using data as reported through 12/31/2010

Maryland Infectious Disease and Environmental Health Administration
March 3, 2011
23

HIV/AIDS: MARYLAND

Reported HIV Diagnosis Trends by Age at Diagnosis MSM Exposure



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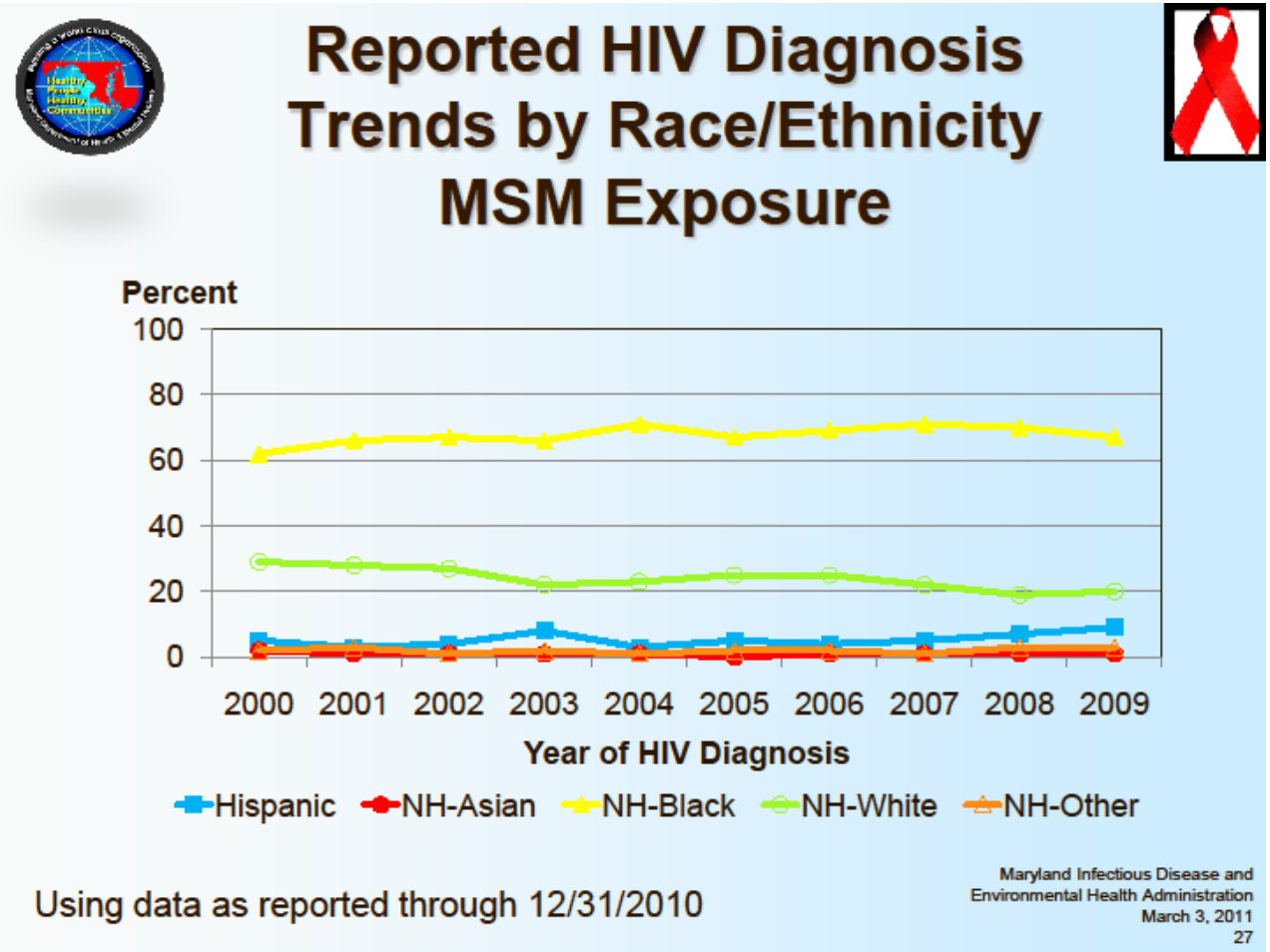
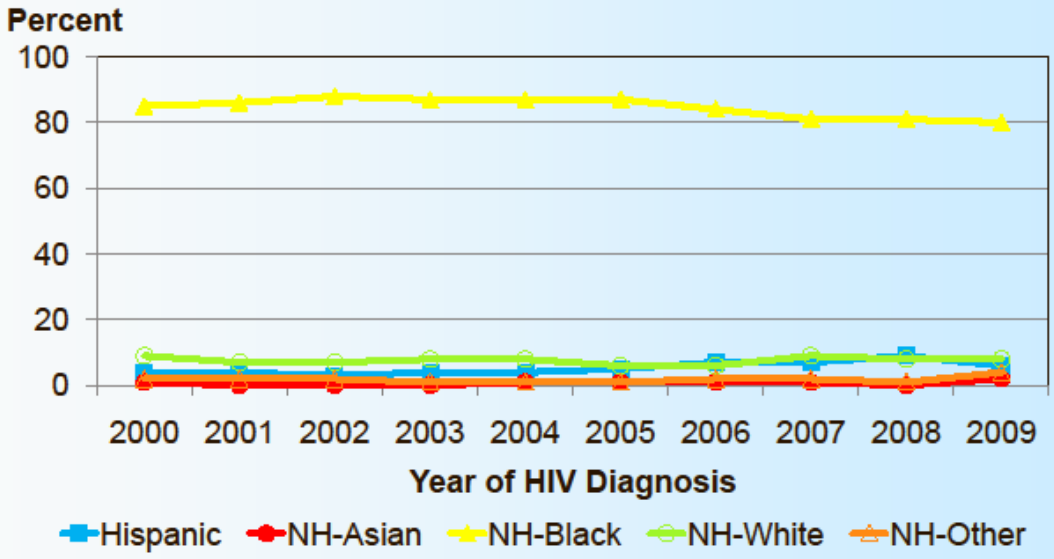
March 3, 2011
28

HIV/AIDS: MARYLAND



HIV/AIDS: MARYLAND

Reported HIV Diagnosis Trends by Race/Ethnicity Heterosexual Exposure



Using data as reported through 12/31/2010

Maryland Infectious Disease and Environmental Health Administration
March 3, 2011

HIV/AIDS: MARYLAND

Rank: #2 state (2010)

Rate: 5 x national average

Regional assets:

- MADAP, DHMH, BCHD
- Clinical services

State of HIV science:

- Treatment (done-Fauci/2008)
- Priorities: Prevention and TLC

Challenges:

- Prevention
- Test → link → retain

WILL WE PREVENT HIV?

- **Rate of new cases in US stable at 50,000-55,000/yr – 1990-present**
- **Prevention Methods:**

  Condoms: Variable usage

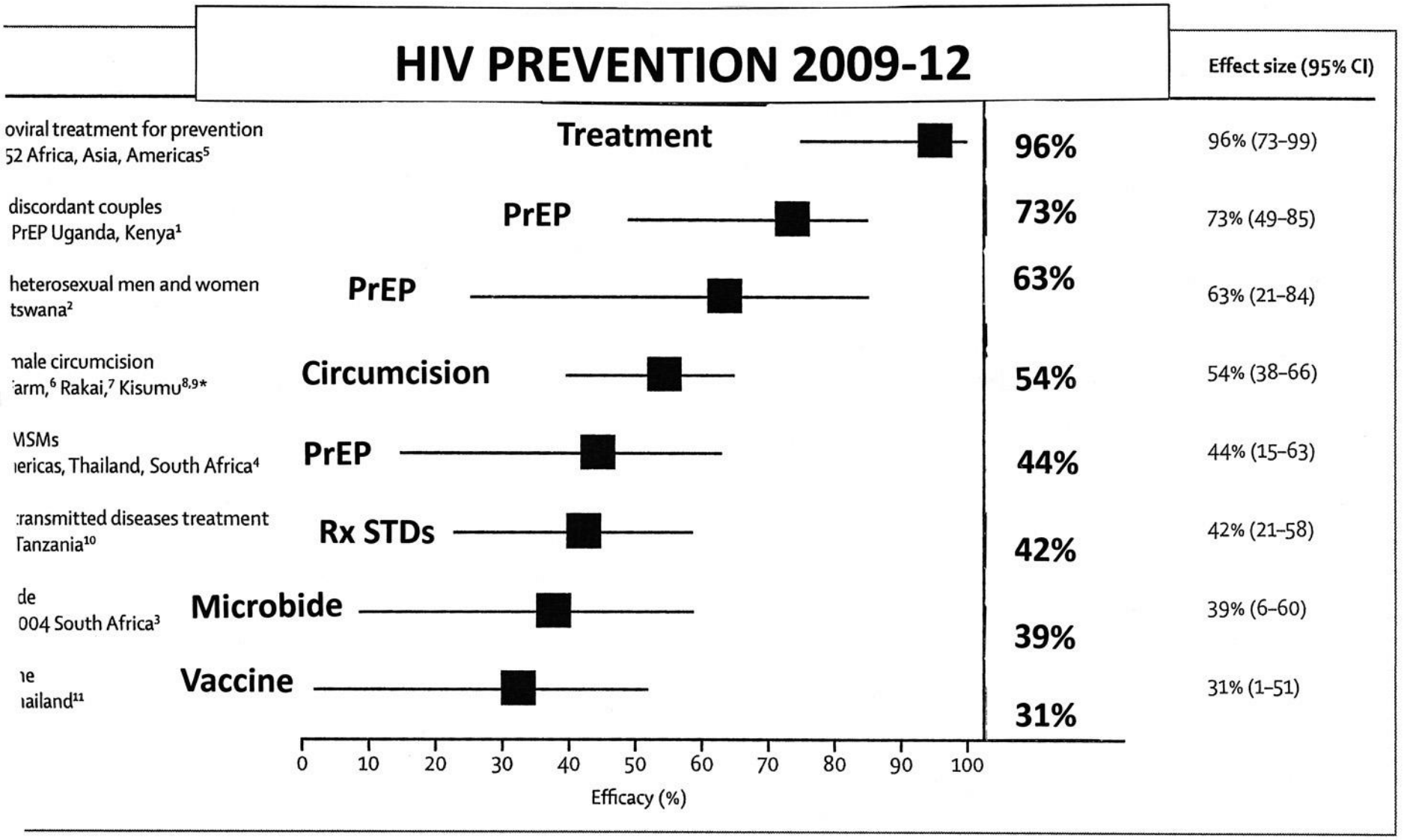
  PrEP (40-90%): Cost/toxicity/adherence

  Circumcision (50%): Not US issue

  Needle exchange: ? Impact

  Vaccine (30%): Rebirth of interest

  ART (96%): Washington DC trial



prevention technologies shown to be effective in reducing HIV incidence in randomised controlled trials[1–11]
posure prophylaxis. *Meta-analysis of circumcision trials.

HIV TREATMENT FOR PREVENTION: HPTN 052 M. Cohen (PI) (Cohen MS. NEJM 2011;365:493)

Protocol: Discordant couples, CD4 350-550: Randomized to ART vs. no ART until CD4 <250

Results: N=1,763 (M=890, F-873)

	ART n=886	No Art n=877
HIV transmission*	1**	27

*Linked cases

**Protection with ART = 96% -- Validity of single case is unclear

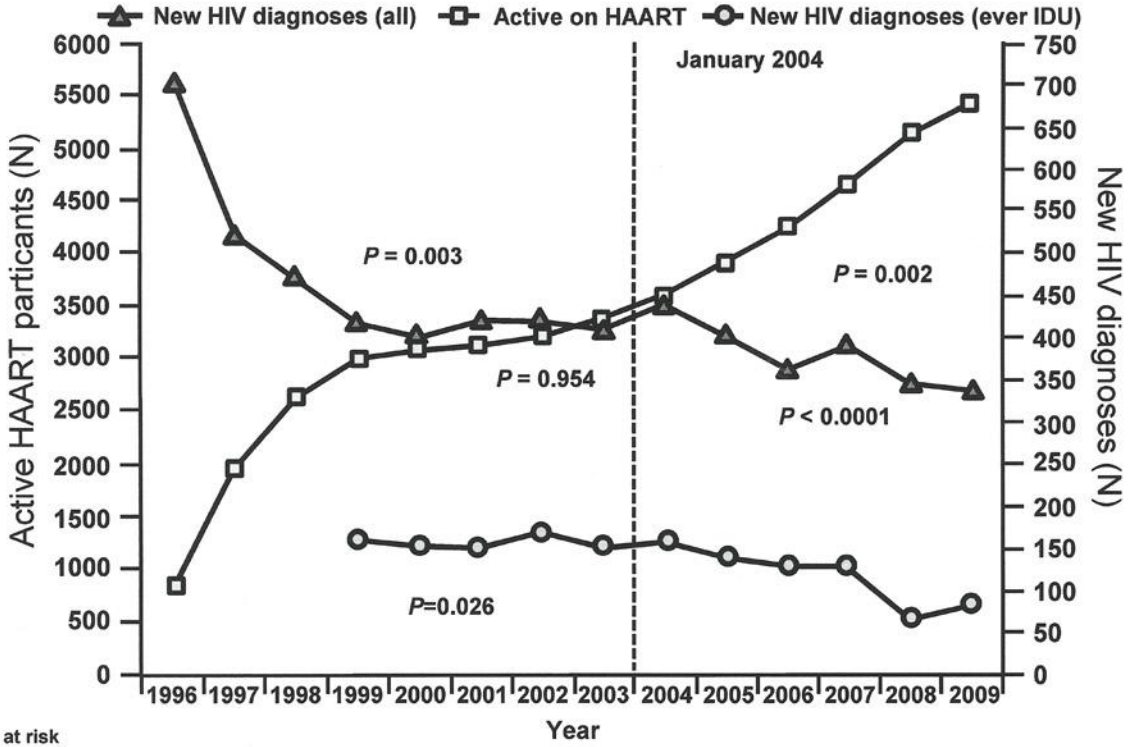
23 December 2011 | $10

Science

BREAKTHROUGH OF THE YEAR

HIV Treatment as Prevention

Effect of Increasing ART on Cases of New HIV: British Columbia



Number at risk														
Active on HAART	837	1960	2597	2994	3079	3120	3211	3356	3585	3913	4255	4654	5123	5413
New HIV diagnoses (all)	702	519	471	416	400	420	418	408	441	400	361	391	346	338
New HIV diagnoses (ever IDU)	NA	NA	NA	159	152	149	168	149	156	137	128	128	65	80
HIV tests done in Bristish Columbia (per 1000)	138	140	137	135	135	135	145	142	154	161	172	176	182	NA

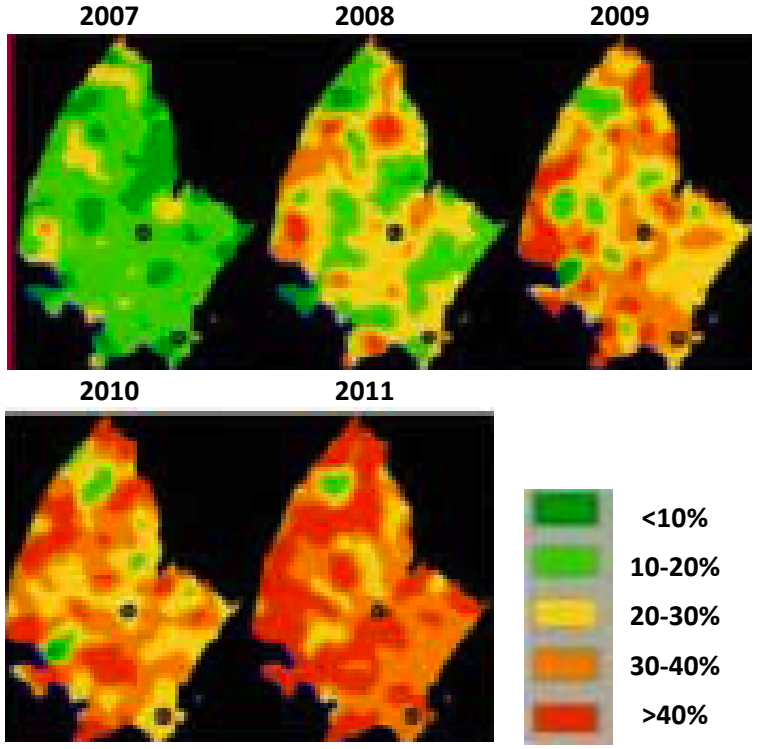
Figure 1: Number of active HAART participants and number of new HIV diagnoses per year in British Columbia, Canada, 1996-2009. *P* values are for trend and were obtained from the generalized additive model. IDU, injecting drug user.

Montaner et al. *Lancet.* 2010;376(9740):532-539. Reprinted with permission.

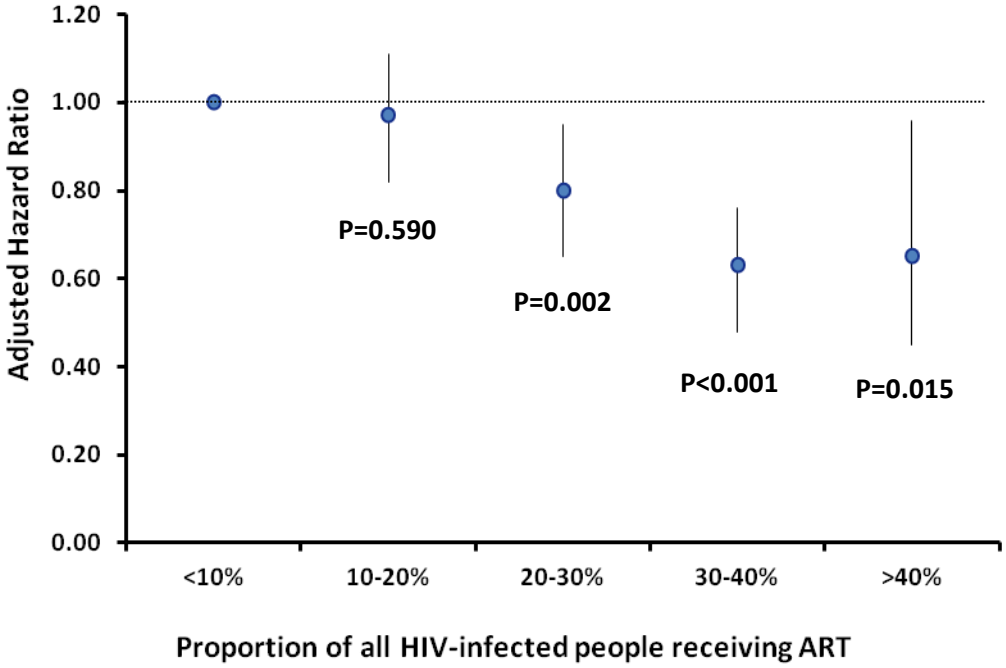
Treatment as Prevention: Effect of ART Coverage on HIV Incidence in Rural South Africa (Tanser F. 2012 CROI;Abstr. 136LV)

- Annual population based HIV surveillance in rural KwaZulu-Natal
- 2004 – 2011: 1395 HIV seroconversions among 16,588 HIV negative adults ≥15 years of age

Spatial Estimates of Proportion of HIV Patients on ART



Adjusted HIV Infection Rate by ARV Coverage Category



Efficacy of Daily Oral FTC/TDF PrEP

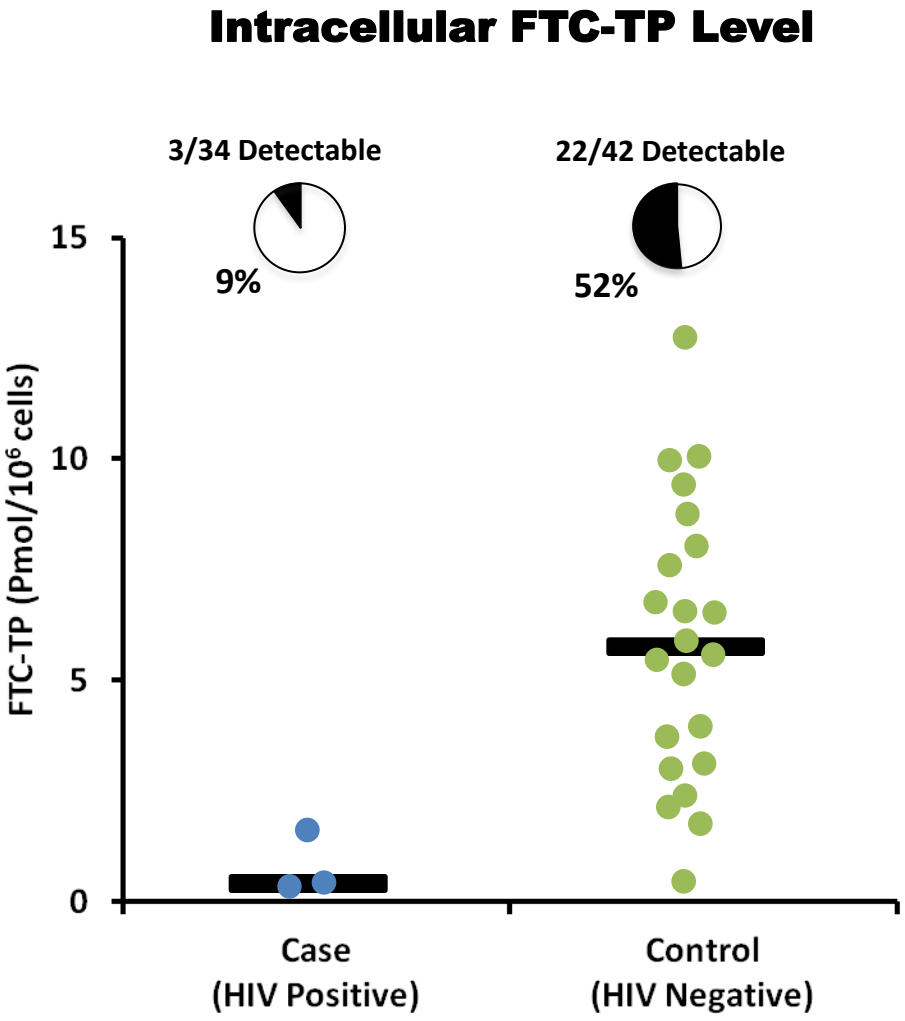
Trial	Pop.	Efficacy	95% CI
iPrEx	MSM	42%	18 to 60%
Partners PrEP	Men	83%	49 to 94%
	Women	62%	19 to 82%
TDF2	Men	80%	25 to 97%
FemPrep*	Women	49%	-22 to 81%
VOICES*	women	TDF only arm discontinued	

*DSMB recommended discontinuation for futility; drug level testing is in progress.

Grant NEJM 2010, Grant IAS Rome 2011, Baeten IAS Rome 2011, Thigpen IAS Rome 2011; FHI Press Release April 18, 2011

Drug Detection Related to HIV Risk in the Active Arm of iPrEx

- **Detection of drug correlated with decreased HIV risk, after controlling for age, risk behavior, education, or BMI (OR 12.9, P<0.001)**
- **92% reduction in HIV risk (95% CI: 71-99%)**



New England Journal of Medicine, online Nov 23, 2010, Anderson IAS Rome 2011, Grant ICAAC Chicago 2011.

CHALLENGES OF PrEP

Adherence: Huge Issue

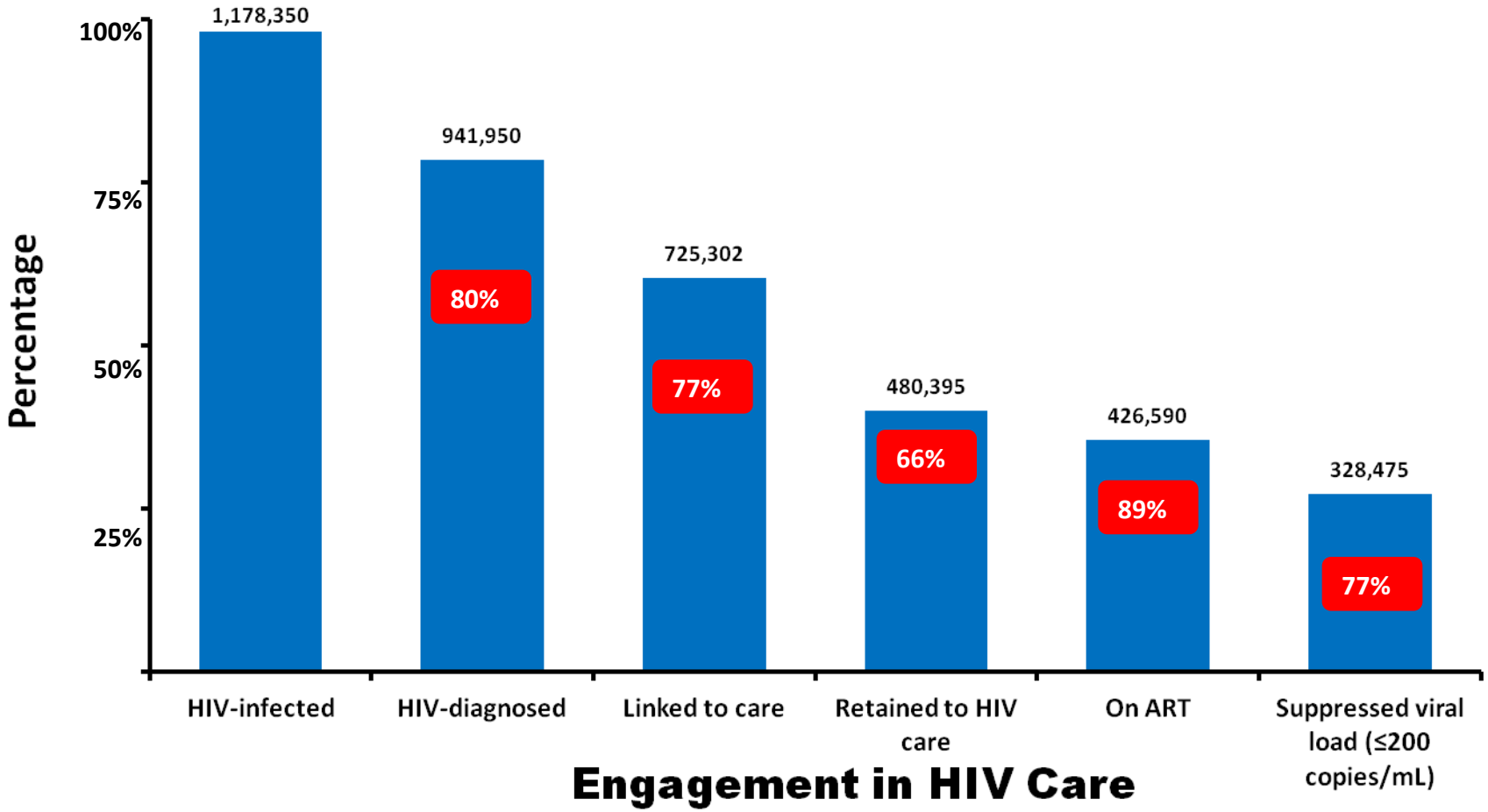
Cost: TDFD/FTC AWP = $1391.45/mo

CDC recs (?): 4 medical visits/yr for ADR and HIV serology

Long term toxicity (?)

What will happen(?): Selective use

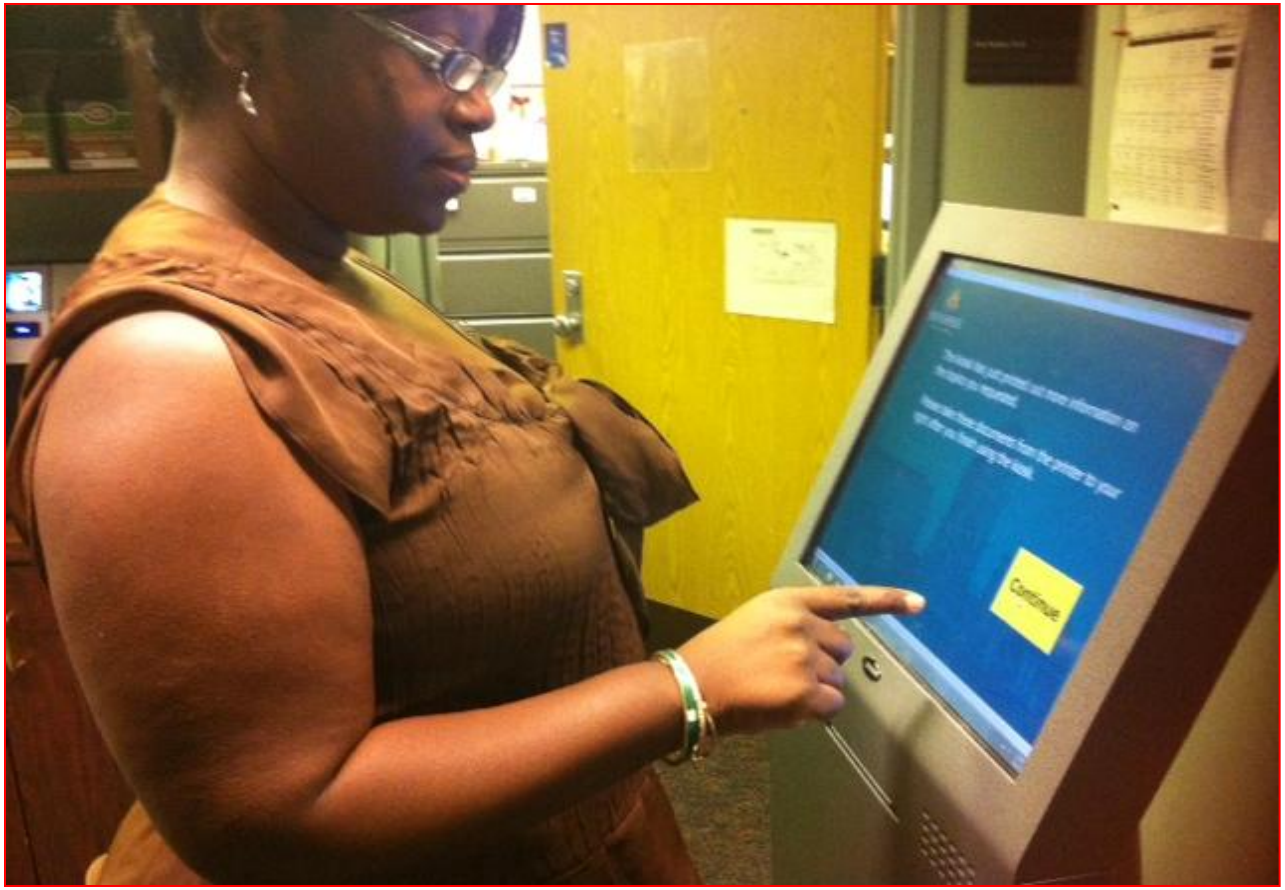
The Continuum of HIV Care -- US



Of all with HIV infection, 850,000 individuals do not have suppressed HIV RNA (72%)

MMWR (60), 2011

CONSUMER AT KIOSK FOR SELF TEST



Do you know HIV status?

Do you want to test yourself?

Potential: GC, CT, Syphilis trichomoniasis, HCV

Detection of *C. trachomatis*, *N. gonorrhoeae* and *T. vaginalis* in dry shipped self collected swabs.

(Gaydos C. Diagn Microbiol Inf Dis 2012;73:16)

Background: New cases/yr US-CT: 3 million; GC – 0.7M, TV – 8M

Method: Self collected vaginal swabs → mailed to the lab (Baltimore to Birmingham) → NAAT test

Detection: 10 organisms

DETERMINE HIV 1/2 Ag/Ab Combo POC TEST (Branson B. JID 2012;205:521)

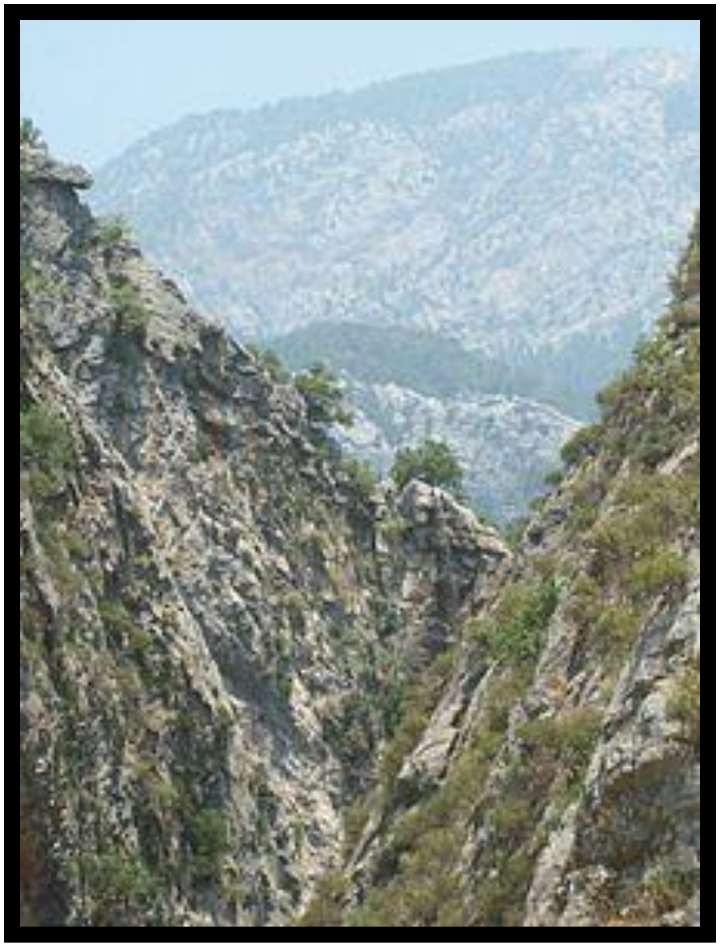
Detects HIV Ab and p24Ag

Advantages

- **POC**
- **Requires no electricity, water or large equipment**
- **Sensitivity with acute HIV (10 days)**
- **Detects HIV-1 and HIV-2**

WHY 30% of persons who test positive for HIV do not know it

HIV Test Positive



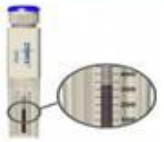
WB

Point-of-Care CD4 Technologies in the Pipeline*

PointCare

PIMA

BD



Zyomyx

Partec Mini

Daktari

mBio

Burnet

2009 2010 2011 2012 2013

Instruments

Disposable

UNITAID

*Estimated; timeline and sequence may change.

P4P4P: THE STATUS OF PAYING PATIENTS FOR SELF CARE

Practice: Widespread and international

Incentives: Cash, groceries, lottery tickets, meal tickets.

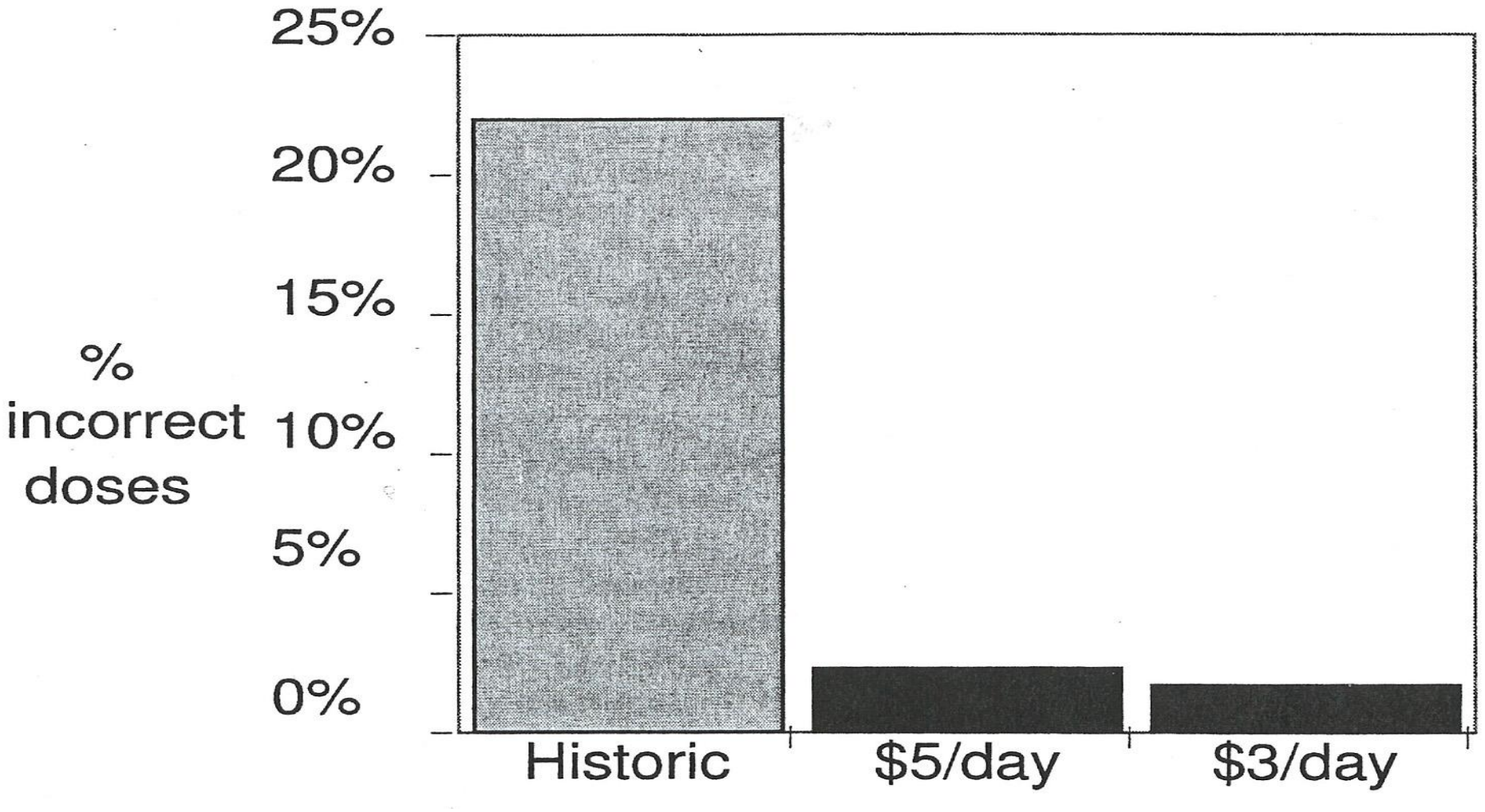
Conditions: Chronic – smoking, obesity , BP control, diabetes, HIV

HIV trial: HPTN 65 – Controlled trial, (unblinded) HIV test – $25, Enroll in care – $70, NDV – $280/yr (1.7% of HIV care cost)

Status: Widely practiced, no one wants to talk about it.

A TEST OF FINANCIAL INCENTIVES TO IMPROVE WARFARIN ADHERENCE

(Volpp KG. BMC Health Sys Res 2008;8:272)



RECOMMENDATIONS FOR WHEN TO START ART
(DHHS Panel on ART 1996-2012)

Year	WHO	CD4*
1996	CD4	<500
2000	CD4	<200
2006	CD4	<350
2009	CD4	<500
2012	All pts	Any CD4 count

COST OF CARE

Contemporary costs/yr.
(*AIDS* 2010;24:2705)

- **HAART – $12,000**
- **Meds – other – $2,100**
- **In-patient – $600**
- **Out-patient – $400**

Total (Meds) –$16,600 (72%)

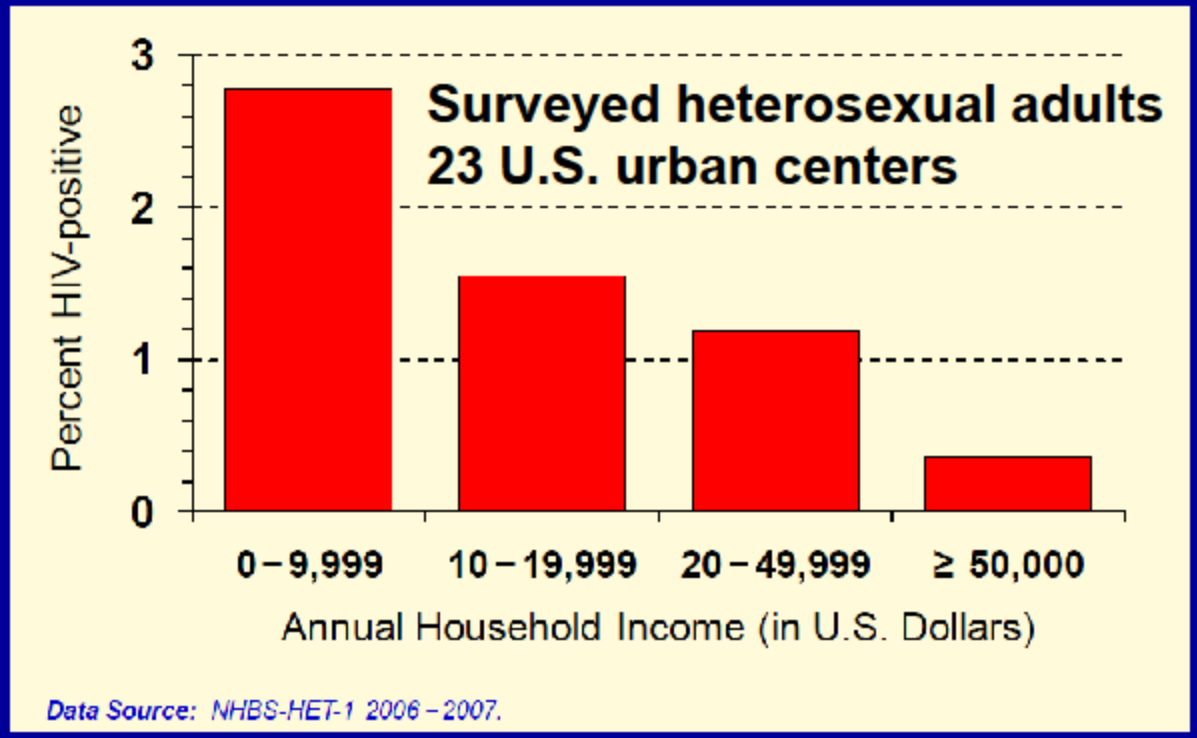
Growth: New infections – 50,000/yr

Deaths – 10,000/yr = 40,000/yr added

Guidelines: Treat all with HIV

Budget: $16K/yr = $16B/yr

U.S. HIV Prevalence Rate - NHBS



Data Source: NHBS-HET-1 2006 – 2007.

Source: Denning at el., AIDS 2010 Conference, Vienna Austria, July 2010, Abstract WEPDD101
NHBS – National HIV Behavioral Surveillance System

HIV Priorities and Plan

Healthcare Reform

HIV Funding

HIV/AIDS IN THE US: 2015 GOALS

Reduce new infections

- Increase known HIV status from 79% to 90%
- Increase testing

Improve access to care

- Link 85% of newly diagnosed patients to care within 3 months
- Increase number in continuous care under Ryan White Care Act

Reduce HIV-related health disparities

- Increase proportion of patients with undetectable VL by 20% in minorities (blacks, Latinos, MSM)
- "Community viral load"

Improve coordinated response

White House Office of National AIDS Policy. http://www.aids.gov/federal-resources/policies/national-hiv-aids-strategy/nhas.pdf. Accessed January 6, 2011

HEALTHCARE OUTCOMES IN HIV: REDUCING DISPARITIES (Moore R. CID; in press)

Issue: Major issue in HIV care is retention in care and adherence

Method: Moore Clinic data 1995-2010

N=6,366 Pt/yrs 27,941

Demographics: B – 77%, F – 34%

Risk: IDU-45%; MSM – 30%

Insurance: Private – 15%

Results: Calculated life expectancy at age 28 yrs = 73.4 yrs for all groups – race, gender and risk

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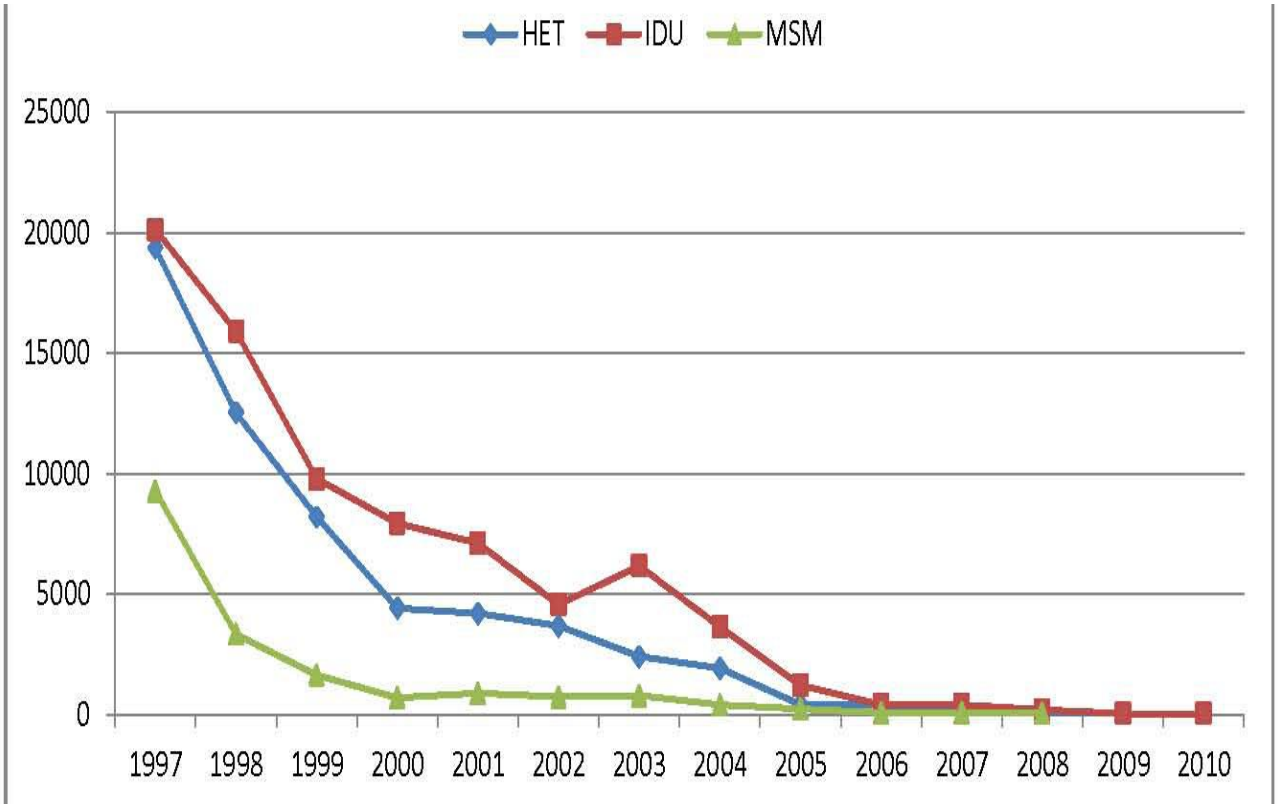
VL FOR 3 HIV RISK CATEGORIES OVER TIME
(Moore RD. CID 2012; in press)



HIV Viral Load

(Median)

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Total (Meds) –$16,600 (85%)
Growth: New infections – 50,000/yr
Deaths – 10,000/yr = 40,000/yr
Guidelines: Treat all with HIV
Budget: $16K/yr = $16B/yr

PRESIDENT OBAMA'S BUDGET REQUEST (4/10/12)

Total: $3.8 trillion for HIV

Content	Current (FY12)	CHANGE
RWCA-ADAP	**$940M**	**+$102M (+10%)**
• **Part C: Primary Care**	**$211M**	**+$20M (+10%)**
• **Part D: Youth/Families**	**$78M**	**- $8M (-10%)**
CDC – disparities	**?**	**+ $40M**
HOPWA	**$330M**	**- $2M (-1%)**
PEPFAR	**$7.1B**	**- $900M (-13%)**
Research	**$3.1B**	**- $100M (-1%)**

WHEN DO CONTEMPORARY (FAVORED) ART AGENTS BECOME GENERIC

FDA approval + 16 years

Years + 16	Agents
2011-	3TC
2012-15	EFV, LPV/r, NVP
2016-18	TDF, FTC, ABC,ATV/r
2019-22	DRV, RAL

HIV PLAN

1. Increase testing
   - Enhance access to testing
   - Screen positive → directly to care
   - Retention: Requires multiple services (P4P4P)
2. ART → reduce community viral load
3. PrEP: Selective use

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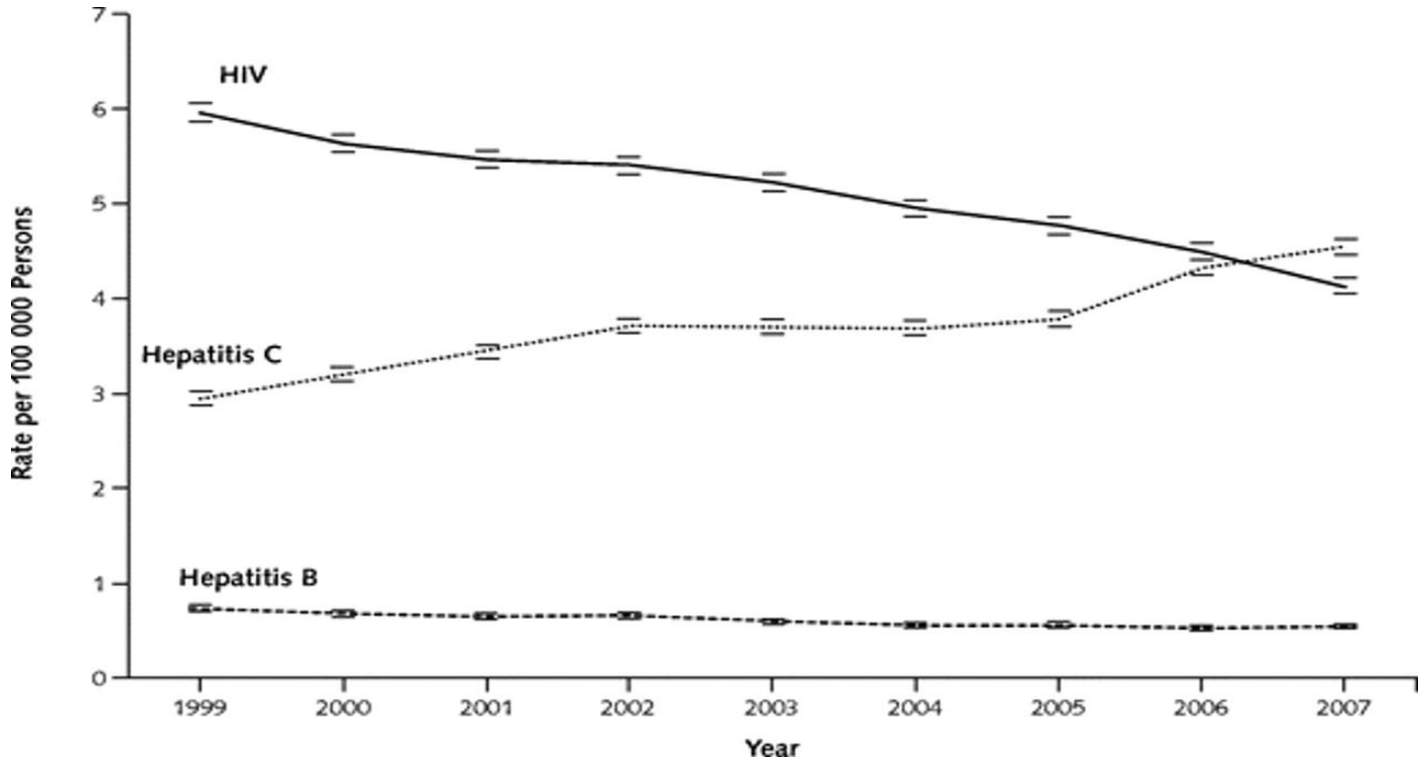
Conclusions

MORTALITY RATES DUE TO HIV, HCV AND HBV IN US 1999-2007 (Ly KN, et al. Ann Intern Med 2012;156:271-278)



HEPATITIS C

Number infected in Maryland: 95,400 (?)

Number who know it: 40-50%

Morbidity: Major cause – cirrhosis, liver cancer, liver transplant (21 deaths/hr)

Why now? Pipeline loaded

CELEBRITIES WITH HCV

Evil Knievel: Motorcycle daredevil

Billy Graham: WWF wrestling champ

Jack Kevorkian: Physician

Laurie Bembenek: Playboy bunny

Rolf Benirschke: San Diego Charger

Mickey Mantle: Yankee player

James Earle Ray: Assassin

Benito Mussolini: Dictator

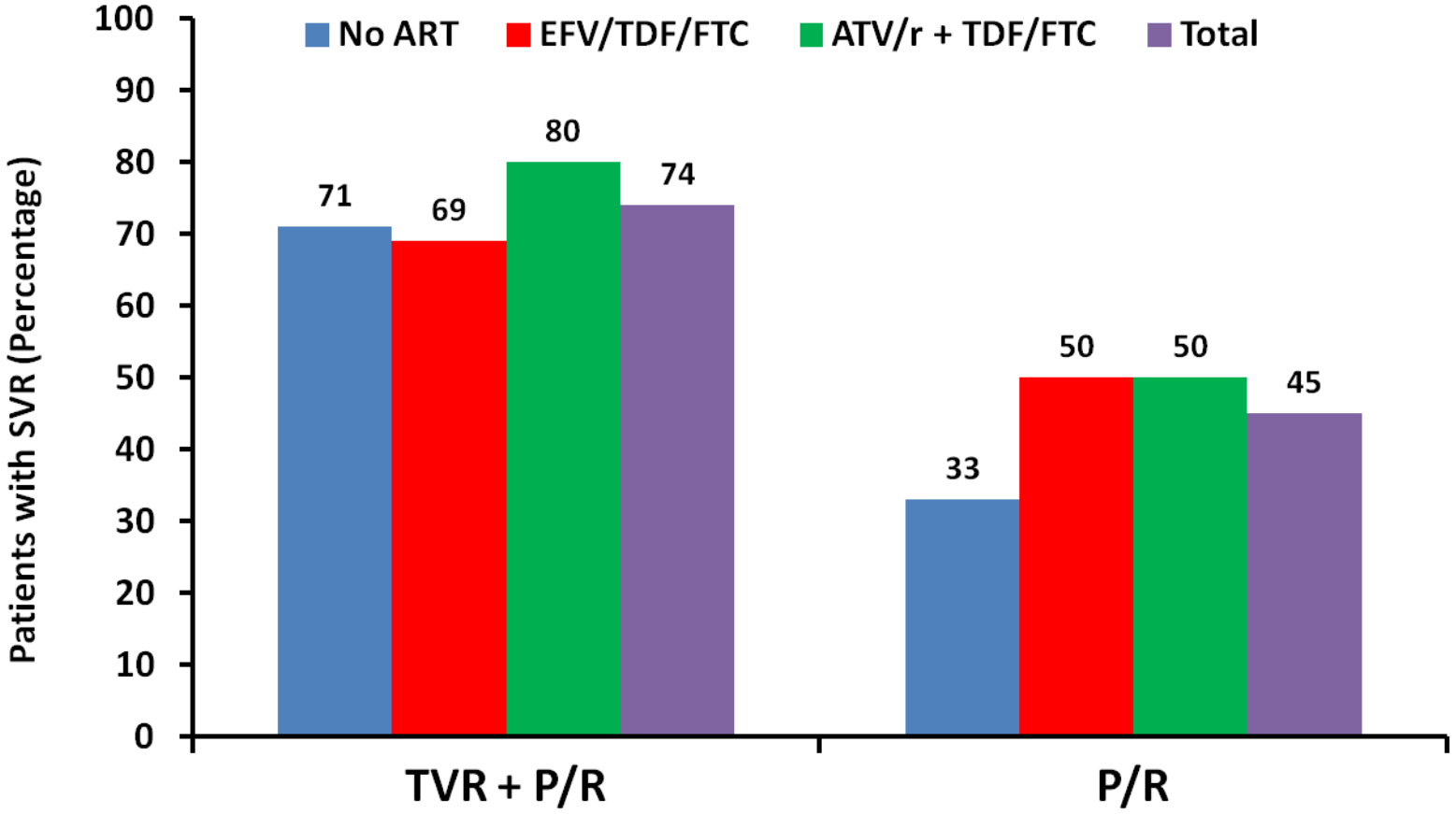
Linda Lovelace: Actress

HOW WILL HCV TREATMENT CHANGE?

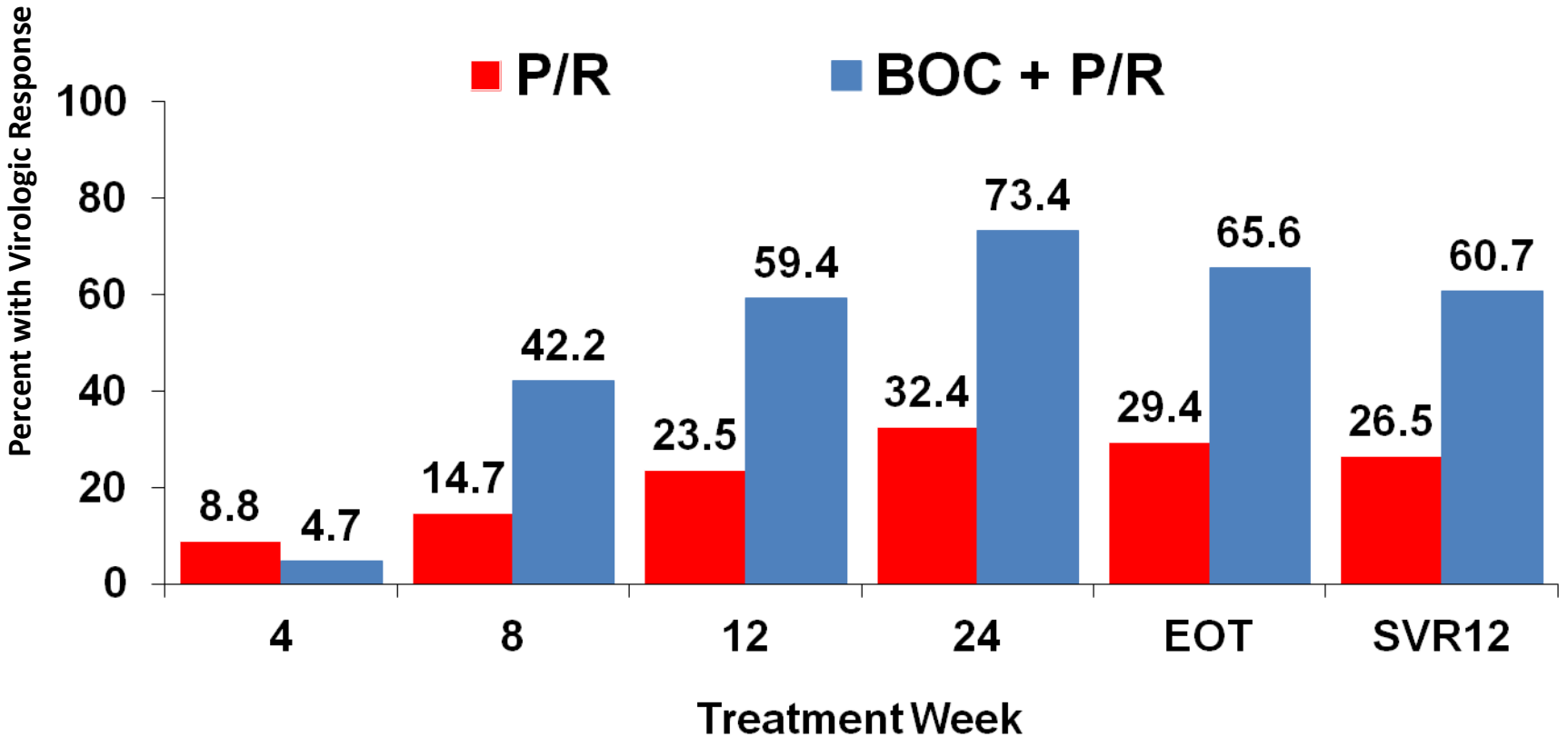
HCV Treatment

- **1991: Interferon**
- **1995: PegINF/rib**
- **2011: PegINF/rib/PI (TPV, BOC)**
  + 57 drugs in development
- **2012: Pipeline – 37 agents**
- **2014: No INF/r, all oral, high cure rates, high cost**

Telaprevir + Peg-IFN and RBV: Sustained Virologic Response (SVR12) (Dietrerich D. 2012 CROI;Abstr. 46)



Boceprevir + Peg-IFN and RBV: Sustained Virologic Response (SVR12) (Sulkowski M. 2012 CROI;Abstr. 47)



HCV DRUG TREATMENT COST (Maryland ADAP data)

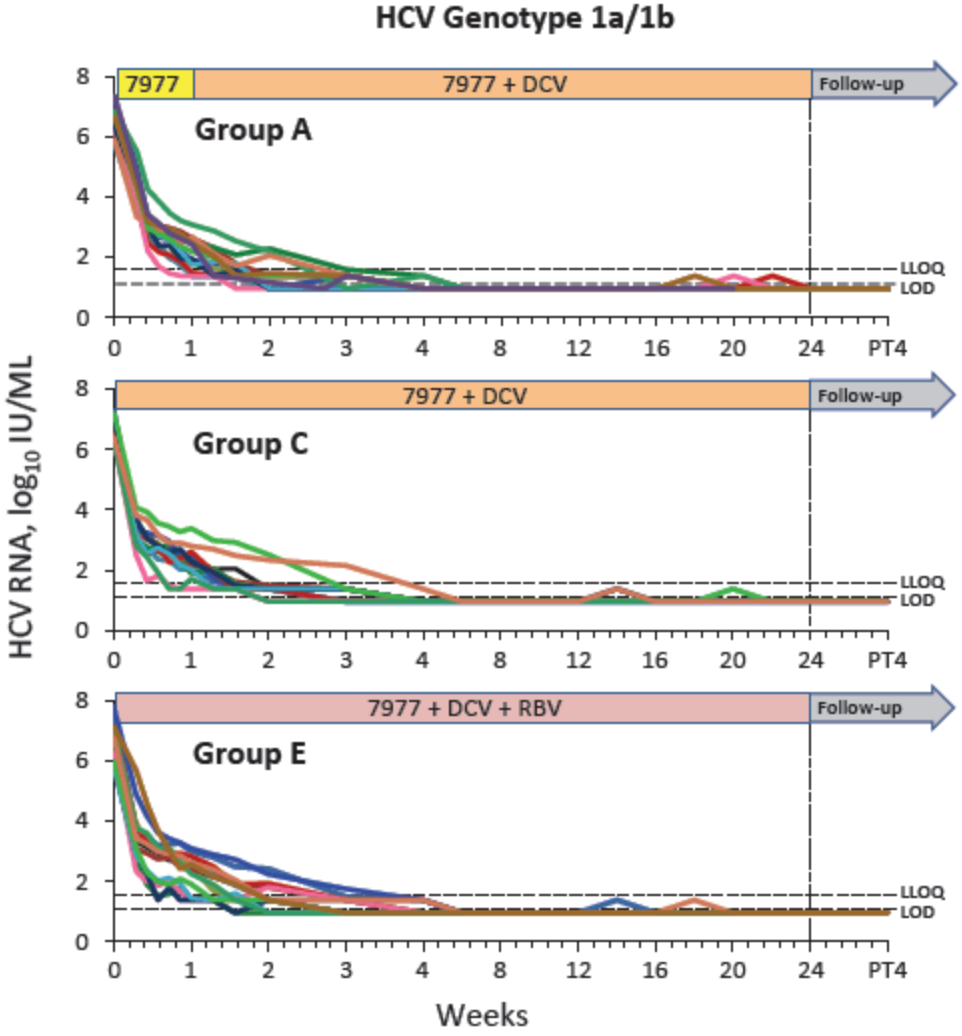
BOC -- $51,116/course (HCV only)

TVP -- $51,957/course (HCV only)

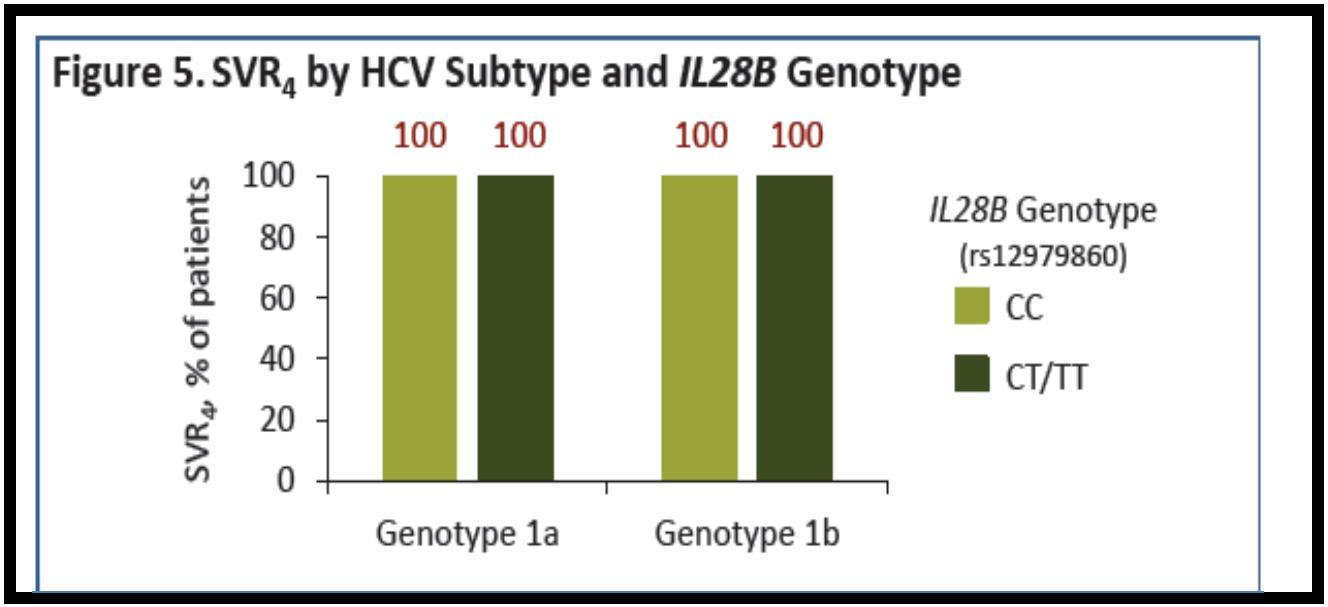
$77,936 with EFV

GS 7977 (NS5B inhibitor) + Daclatasvir (NS5B inhibitor in 44 patients with HCV GT1 (Sulkowski M. 47th EASL, Barcelona 4/18/12)

Figure 3. HCV RNA Over Time – Individual Patients



Oral combinatin GS 7977 + Daclatasvir + ribavirin in patients with HCV GT1 (n=44) (Sulkowski M. EASL, Barcelona, 4/18/12)



EUROPEAN ASSOCIATION FOR STUDY OF LIVER DISEASE (EASL) MEETING SUMMARY (Pawlotsky J-M. 4/22/12, Barcelona Spain)

HEPATITIS C

Testing:

- **Screening: All at risk and all born 1946-64 (CDC)**
- **HCV-Ab → VL, genotype, LFT → Refer**

Treatment: Now or later?

Decision – Fibrosis score and cost/trials

STI'S:
WHAT'S ON THE HORIZON

Overview

Epidemiology

Gonorrhea

HIV/AIDS

Hepatitis C

Human Papilloma Virus

Conclusions

HPV VACCINE: CDC recs 2012

Vaccines: Cervarix (HPV2) 16/18
Gardasil (HPV4) 6/8/16/18

Recommendations

- Females: HPV2 or HPV4; 3 doses at age 11-12, catch-up 13-26
- Males: HPV4; 3 doses at age 11-12, catch-up 13-26
- Immunocompromised: To age 26
- MSM: HPV4 to age 26

EARLY EFFECT OF HPV VACCINE ON CERVICAL ABNORMALITIES IN VICTORIA, AUSTRALIA

(Brotherton, et al. Lancet 2011;377:2085)

Issue: Australia – quadravalent HPV vaccine for women 12-26 yrs 2007-09 – ? Impact

Method: Cervical cytology Registry data for 2003-09 vs. 2007-09

Results: Significant decrease in incidence of high grade cervical abnormalities in girls <18 years

TRENDS IN INCIDENCE: HGCA (Brotherton, et al. Lancet 2011;377:2085)

	Age <18		Age 18-20	
	Incidence	P	Incidence	P
Pre-vaccine	0.99		0.99	
Post vaccine	0.87		1.00	
Before vs. after	1.14	0.05	0.99	NS

Note the importance of early vaccine

Potential: Cervical cancer – 529,000/yr – 85% in developing countries

HPV VACCINE AGAINST ANAL HPV INFECTION AND ANAL INTRAEPITHELIAL NEOPLASIA

(Palefsky JM. NEJM 2011;365:1576)

Issue: 1) HPV 16/18 are highly associated with anal cancer; 2) anal cancer rates increasing and 3) MSM are at high risk

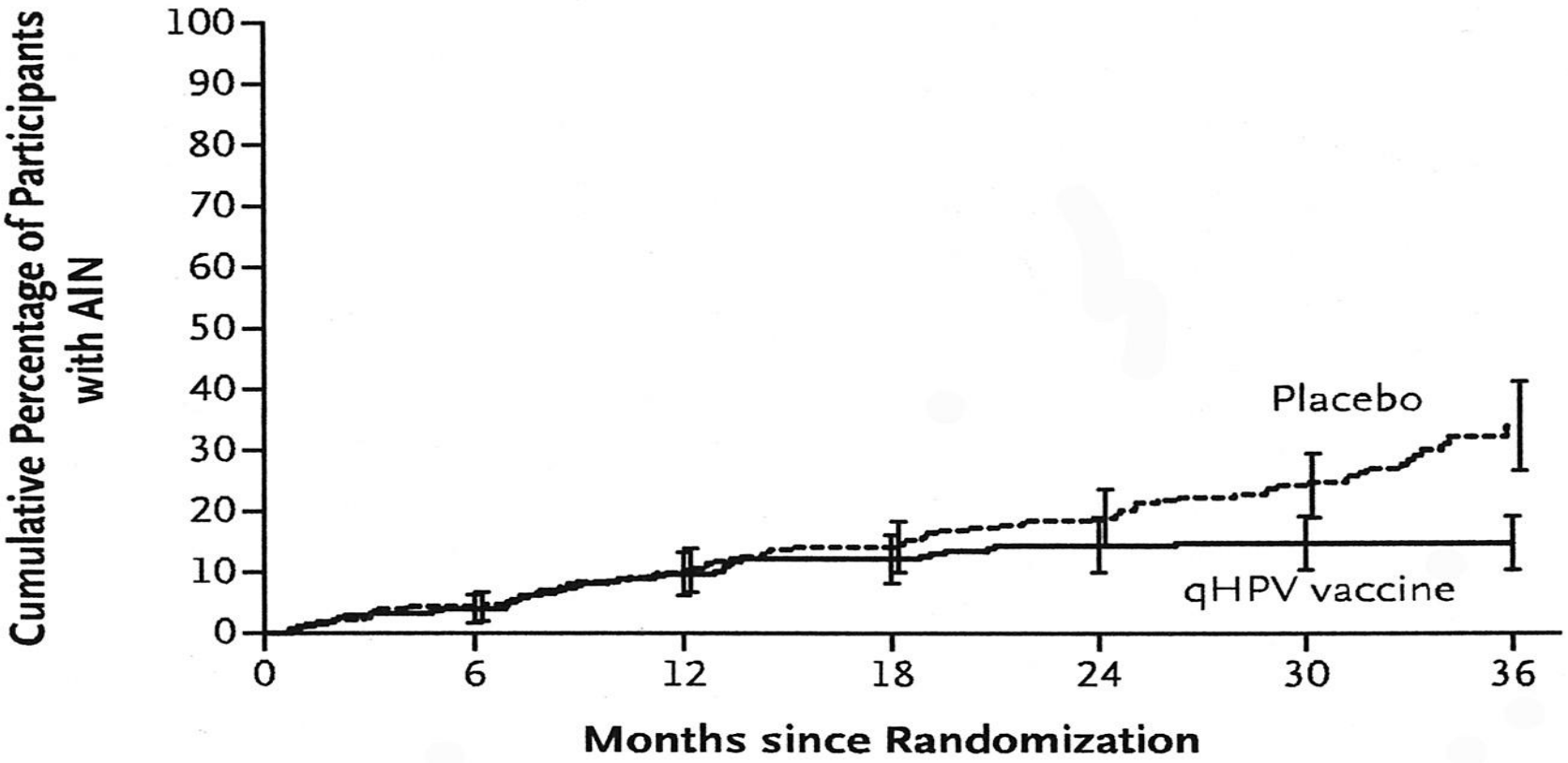
Method: Double blind randomized trial HPV vaccine for 608 MSM (ages 16-26). Efficacy based on anal intraepithileal neoplasia (AIN) and anal cancer

Results: Rate of grade 2/3 AIN reduced 75%; rate of infection reduced 49%

INCIDENCE OF HPV-6, 11, 16, OR 18 RELATED AIN.

(Palefsky. NEJM Year; 268;365:1576)

B HPV-6, 11, 16, or 18–Related AIN in the ITT Population



No. at Risk							
qHPV vaccine	275	264	225	208	191	148	45
Placebo	276	263	236	218	192	146	38

Palefsky: Answers and Comments

Why HPV 6 & 11?

May cause some low grade AIN but "Cervirax should be just as good"*

***Note: Survey of teenagers – far greater concern for genital warts**

Age limit of 26 in MSM?

Agree with CDC but "reasonable to individualize"

VACCINES: COST (AWP-2012)

Vaccine	Cost Single dose	Vaccine Rates
HPV Gardasil Cervarix	$155 (x3) $134 (x3)	21% (F)
Influenza	$ 32	44%
Pneumococcal Pneumovax Prevnar 13	$ 74 $145	60% (>65 yrs) ——
Zoster	$192	14%
Tdap	$ 47	

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STIs: CURRENT STATUS

Strengths: Commitment and resources – STIs, HIV, HCV

Issues:

- STI rates: Race/MSM/City
- Antibiotic-resistant GC
- HIV: Test, TLC & Retain + Community VL
- Resources: CDC, AETC

Eureka: Public health led effort via statewide public health/ID services

Thank You

Patrick Chaulk

Colin Flynn

Khalil Ghanem

Heather Hauck

Ned Hook

Elizabeth Liebow